COUGH SYNCOPE

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By

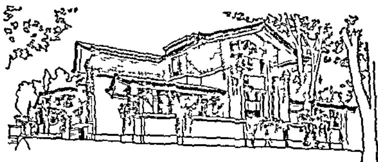
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Helpful suggestions have also been received from our Editor and from our Publisher

V J D
A K

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COUGH SYNCOPE

CHAPTER I

Introductory

A INTRODUCTION

The syndrome of syncope following cough has been reported under a variety of terms Some of these have been inapt and have resulted in attention being diverted away from the main clinical features of the syndrome Because of this diversity of terms reports have appeared in the literature of various interests such as otolaryngology neurology psychiatry pediatrics and general medicine Until very recently the literature of internal medicine has been singularly lacking in attention to the entity There is found nowhere in the American literature a reasonably complete presentation of this curious and rather rare condition Because of this the authors have undertaken a critique of this entity and its related aspects Twenty five cases coming under the authors personal observation will be reported together with an additional ten cases made available to them through the courtesy of colleagues It is 50 years since a series of comparable size has been reported (Moncorgé 1902 (234 and 235)) A brief discussion of topics pertinent to this syndrome such as fainting epilepsy narcolepsy the laryngeal crises of tabes dorsalis voluntary death by breath holding and the medicolegal aspects of the syndrome are included

As indicated later the bulk of the literature pertinent to this syndrome is found in foreign writings We have been

fortunate to obtain, in nearly all instances, the original references and it has been possible for us to translate these directly As might be anticipated when writings occur in many languages there have been discovered many, not always minor, errors in interpretation which have been perpetrated It is our hope to correct the major ones of these

From the review of the literature, from the study of our observed cases, and from a consideration of the mechanism involved, a fairly distinct clinical picture has evolved

B DEFINITION AND TERMINOLOGY

We choose to define the syndrome under discussion in a direct fashion it shall consist of the occurrence of loss of consciousness which is preceded by coughing There may be, in certain instances, accompanying convulsions Episodes of coughing followed only by dizziness, light headedness, or a sense of unreality are thereby excluded What error, if any, may ensue from this limited definition, it is believed will be compensated for by clarity Episodes of syncope and related states not preceded by cough, even though they occur in subjects who faint after coughing—and this combination is a rare occurrence—are likewise excluded by definition

From the standpoint of medical nosology the entity cannot be considered as a disease since many causes may produce the clinical picture It, however, can justify the application of the word syndrome, since it is a symptom complex or a combination of symptoms in a disease (66) In any event to us it presents a characteristic phenomenon, coughing followed by fainting, which often appears in a certain clinical setting

The names given to the syndrome have been

laryngeal vertigo
vertige laryngé
laryngeal ictus
ictus laryngé
laryngeal epilepsy
laryngeal apoplexy
chorea laryngis
lipothymia laryngea
lipothymie laryngée
laryngeal syncope
Kehlkopfschwindel
Larynxcrisis
spasmus glottidis adultorum
complete glottis spasm in adults
a rare form of laryngeal neurosis
ictus primitif
ictus idiopathique
ictus essentiel
ictus secondaire
ictus symptomatique
laryngoplegie
bronchial syncope
Larynxschwindel
la toux obnubilante
accident laryngé
la toux vertigineuse
laryngisme de l'adulte
apoplektiforme Bewusstseins verluste bei kramphaften Husten
Halsneurose
spasme apoplectiforme du larynx
laringismo inhibitorio
the cough syndrome
tussive syncope
post tussive syncope
tussigenic ictus
bronchial ictus

Of these it is believed the most appropriate terms are the cough syndrome (Baker (19)), tussive syncope (McCann (221)) tussigenic syncope (Lian (203)), and post tussive syncope (Flindt (124)) The term of Baker is admirable for simplicity but does not imply the occurrence of fainting its modification to cough syncope is believed preferable The terms cough syncope cough syndrome tussive syncope tussigenic syncope and post tussive syncope will be used interchangeably throughout. In agreement with many others our strongest objection is to the term by which the syndrome was first known and unfortunately still used in certain quarters, that of laryngeal vertigo Neither of these words being appropriate the term should be abandoned

C HISTORY

At the November 19 meeting of the Societé de Biologie in 1876 Jean Martin Charcot (1825–93 (67)) reported the first case of fainting following cough The minutes of this meeting were published in both the *Comptes Rendus* and the *Gazette Médicale de Paris* A translation of the account follows

M Leven reported a case of rapid death after thoracentesis

M Charcot à propos of the communication of M Leven, spoke of a series of facts which he has observed which he believes to be little known

"M Charcot was called to see a patient who complained of gout and cough One day, following a mild paroxysm of coughing he saw the patient suddenly sink down upon himself and get up again, without having presented the slightest sign of convulsions The patient after the crisis was over, assured him that he had not lost consciousness and informed him that from time to time he suffered from these accidents ever since the onset of the cough It is unnecessary to add that this patient aged 55 years had never presented the slightest symptoms of epilepsy

Shortly afterwards M Charcot saw with Dr Carrere a 54-year old man—also non epileptic—who complained of having had what he called attacks for a year This state is announced by *a tickling below the larynx a little dry cough which is fol* lowed at times by a sort of attack during which the patient falls and loses consciousness During this attack, according to state ments of those who have been able to witness this it appears that his *face becomes violaceous turgescent and there are* several convulsive movements of the head and arms He does not bite the tongue nor urinate The attack is short and scarcely is it over when the patient arises, perfectly clear and *even finds himself capable of continuing the conversation* which began before the attack These attacks have become very frequent for some time there are 15 to 16 a day and it

has happened that the patient has fallen in the street. Each time the attacks have been preceded by tickling and a little cough however it may happen that these attacks of coughing are not followed by the complete attacks In this case the patient only feels a vertiginous sensation which he is unable to define but which is never accompanied by falling

"The examination of the throat revealed a little granular pharyngitis The patient has for a long time suffered from chronic bronchitis and emphysema but it is only for the past year that these attacks have occurred

"M Charcot has been led to think that in these cases one may be dealing with irritation of the laryngeal nerve in the same way as the vertigo alluded to as Ménière s disease may be referred to an affection of the auditory nerve in the labyrinth. It would be thus a sort of laryngeal vertigo Under this impression he prescribed pharyngeal cauterization with silver nitrate, irritating applications to the laryngeal region and internally the use of potassium bromide Whether because of the effect of this medicine or whether due to an entirely different cause the patient recovered at the end of several months"

Although Charcot called attention to the entity in a series of reports (67 68 and 69) it is certain that its occurrence was known to other physicians The notations of Sydenham (1624–89 (318)) and Heberden (1710–1801 (159)) illustrate this point Parkes (263) attributes the first instance of "laryngeal epilepsy" to Sydenham Our reading of the original indicates rather that Sydenham was describing only the vertigo which appeared in an epidemic of upper respiratory tract disease believed by later observers to have been influenza His use of the word vertigo is as follows *"aliae vero pulmones ita vehementer agitabant vertigine insuper correptus"* Sydenham s use of the phrase *tussis convulsiva* describes the type of cough seen in these patients and not the occurrence of convulsions after cough The description

Decreasing acuteness of lesions →

WET DRESSINGS →	LOTIONS LINIMENTS →	CREAMS OINTMENTS
weeping	edema	scaling
heat	heat	lichenification
edema	chapping	pruritus
crusting	pruritus	infection
pruritus	infection	erythema
infection	erythema	
erythema		

Schematic Presentation of Indications for Topical Treatment

Acne Preparations

TREATMENT OF ACNE VULGARIS includes the use of both topical and systemic medications Topical therapy and ultraviolet light help control the seborrheic component and follicular plugging Systemic antibiotics inhibit the growth of micro-organisms Oral administration of estrogens and exposure of the skin to x rays decrease sebaceous gland activity Choice of treatment depends in part on the extent and severity of involvement and the age and sex of the patient X rays systemic antibiotics and estrogens are usually very effective agents However they have definite limitations because their effects are not lasting they may be expensive and they may have undesirable side reactions For these reasons it is important to concentrate on topical means of therapy with or without ultraviolet light even though the effects of these measures are not as dramatic as those of other modalities

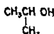
For mild acne (seborrhea comedones few papules) only local therapy is indicated For moderate acne (much seborrhea many comedones papules and pustules) topical measures should be used vigorously On occasion antibiotics x rays and estrogens may be tried For severe cases (cysts in addition to milder lesions) surgical drainage is often indicated In addition to local therapy antibiotics estrogens or x rays may be given Steroids are used topically if a marked inflammatory component is present.

TOPICAL PREPARATIONS

The ingredients of topical medicaments consist of some form of sulfur salicylic acid resorcinol ethanol propanol and acetone A great variety of commercial preparations are available Only a few will be mentioned here.



Ethanol

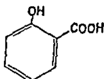


Isopropanol

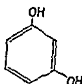


Acetone

These organic solvents can be applied to the skin in order to remove secretions from the orifices of sebaceous glands. Ethanol and acetone have an advantage over isopropanol in that their boiling points are low, hence the skin dries rapidly after they are applied.



Salicylic acid



Resorcinol

Salicylic acid and resorcinol are keratolytic agents which reduce follicular plugging.



Sulfur

At least three different types of sulfur are used pharmaceutically: precipitated, sublimed and colloidal. All forms are over 99% pure. Precipitated sulfur exists in a finer state of subdivision than sublimed sulfur. Precipitated sulfur is microcrystalline or amorphous, while sublimed sulfur occurs as larger crystals. The particle size of colloidal sulfur is even smaller than that of precipitated sulfur. Sulfurated potash is a mixture of potassium polysulfides and potassium thiosulfate. It contains not less than 12.8% sulfur in combination as sulfide.

When sulfur comes in contact with the skin a chemical reaction occurs so that hydrogen sulfide and sulfur containing acids are formed. These sulfur compounds inhibit the growth of microorganisms. They have a drying action on the skin and may decrease the activity of sebaceous glands.

Sal Alcohol

Salicylic acid 1%
In 70% ethyl alcohol

Isopropyl alcohol can be substituted for ethyl alcohol. However ethyl alcohol evaporates faster than isopropyl and is more comfortable to use.

Sebasum (Summers)

Ethyl alcohol	50 %
Acetone	14 %
Polysorbate 80 (Tween)	1 3%
Perfum and coloring agents	0 9%
Distilled water	33 8%

Available in 4 oz bottles

Seba Nil (Texas Pharmacal)

Ethyl alcohol	50 %
Acetone	
Hexachlorophene	0 25%
Sorbitan monolaurate	

Available in 8 and 16 oz bottles

S A R. Lotion

Salicylic acid	0.5%
Resorcin	5 0%

In 70% ethyl alcohol or isopropyl alcohol

Available on prescription.

Application Sal alcohol Sebasum Seba Nil and S A R lotion should be applied with cotton to the involved areas 2 to 4 times daily

Lotio Alba (White Lotion) N F

Zinc sulfate	4%
Sulfurated potash	4%

In distilled water

Lotio alba must be freshly prepared every 3 months Apply nightly

Pronac (Fougera)

Zinc sulfate	0 4 Gm
Sulfurated potash	0 6 Gm

The above contents of one envelope should be mixed with 1 tablespoon of water and applied to the face at bedtime This is an easy way to prepare lotio alba freshly for use each night.

Available in boxes of 12 and 100 envelopes.

Lotioblanc (Arnar Stone)

This preparation contains the same ingredients as lotio alba, N F, plus inert stabilizing agents to keep the suspension uniform Apply nightly

Available in 4 oz bottles

Vleminckx' Solution, N F 10th ed

Lime	16 5%
Sublimed sulfur	25 0%
In water	

Dissolve 1 tablespoonful (16 ml) in 1 pt of hot water to make 1 32 solution Use as a hot wet compress nightly

CaO
Lime (Calcium oxide)

In water, calcium oxide is converted to calcium hydroxide

Available on prescription

Vlem Dome (Dome)

Calcium pentasulfide	60 5%
Calcium thiosulfate	4 5%
Sulfur	4 5%
Inert materials	30 5%

Dissolve contents of 1 packet in pint of hot water and apply as hot compress for 15 minutes nightly

Available in boxes of 12 and 100 envelopes

Sulpho Lac Cream (Kelgy)

Modified Vleminckx solution	57%
Zinc sulfate	23%
Glycerin	3%
Colloidal sulfur	1%
Inert material	2%
Distilled water	14%

Apply nightly

Available in 1, 2 and 4 oz jars

Acne Make up

Acnomel (Smith, Kline & French)

Cream

Sulfur	8 %

Resorcinol	2 %
Hexachlorophene	0 25%
In flesh tinted water washable base	

Available in 1½ oz tubes

CAKE

Sulfur	4 %
Resorcinol	1 %
Hexachlorophene	0 25%
In flesh tinted cake base	

Available in 1 oz. compact.

Resulin (Almay)

LOTION

Sulfur	8%
Resorcin	4%
In a lotion	

Available in 4 oz bottles in regular and half strengths and in blond and brunette shades

OINTMENT

Sulfur	4%
Resorcin	2%
In a vanishing cream base	

Available in 1½ oz tubes in blond and brunette shades

Acne Dome (Dome)

CREAM OR CAKE

Sulfur	8%
Resorcinol monoacetate	6%
2 2 thiobis (4 6-dichlorophenol)	1%
In a water washable ointment or cake base	

Available as cream in 1 oz tubes and as cake in compacts in regular and half strengths and in medium and medium-dark shades.

STEROIDS

Several preparations are available containing sulfur compounds with steroids for the treatment of the inflammatory component of

acne However, the steroid concentration often is low, being 0 25% hydrocortisone It may be advisable to use steroid lotions or ointments containing 1% hydrocortisone or 0 1% triamcinolone acetonide Acute acne cysts may be treated by injection of hydrocortisone solution available for intramuscular use

Soaps

Sulfur containing soaps can be used to aid in the treatment of acne These are listed in the section on Soaps, Shampoos and Baths

SYSTEMIC AGENTS

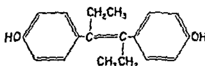
Antibiotics

For moderate to severe acne it is often advisable to give a course of antibiotic therapy in order to bring the disease under control Subsequently, local therapy may be sufficient to maintain a fair state of remission After a few months another course of treatment may be indicated

Broad spectrum antibiotics, particularly the tetracyclines, are usually the agents of choice 250 mg 3 or 4 times daily for 7–10 days

Estrogens

Whereas progesterone and testosterone cause increased sebum levels and exacerbation of acne, estrogens suppress sebaceous gland activity and are sometimes helpful in severe acne Commonly used substances are diethylstilbestrol or Premarin (water soluble estrogens from pregnant mares urine) The schedules given below may be tried for 3 to 6 months



Diethylstilbestrol

Dose for females Premarin 0 625–1 25 mg, or diethylstilbestrol 0 25–1 0 mg daily by mouth beginning with the 14th day of the menstrual cycle and discontinuing hormones the day before the expected on et of menses so that menstruation can occur

Dose for males The above hormones may be given for short periods such as 10 days of each month with complete cessation of estrogens if undesirable side effects such as gynecomastia or impotence occur

Available as diethylstilbestrol in 0 25 0 5 and 1 mg tablets and as Premarin in 0 625 and 1 25 mg tablets

Anesthetics for Topical Use

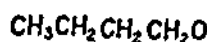
THERE IS A NEED for topical anesthetic agents with a low incidence of sensitization Nupercaine is effective in some disorders but unfortunately it is highly sensitizing Dyclone and Quotane have been promoted as differing from the caine anesthetics It is of interest to compare the structural formulas of these two substances with those of procaine and Nupercaine It will be noted that some similarities exist The e tructures also are related to the antihistamines and some of the tranquilizers Dyclone has been singled out as having anti eptic as well as ane thetic proper ties. These agents are applied 2 to 4 times daily Dyclone solution may be used as a wet dressing

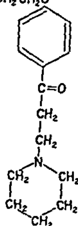
Dyclone (Pitman Moore)

0 5% solution in 1 oz bottles and 1% cream in 1 oz tubes

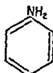
Quotane (Smith Kline & French)

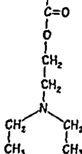
0.5% Quotane in a water washable ointment base in 1 oz. tubes and 0 5% Quotane with 0 1% menthol in a lotion in 2 oz. bottles.



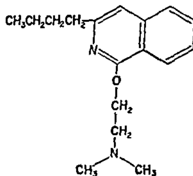


Dyclone

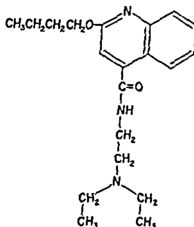




Procaine



Quotane



Nupercaine

Antihistamines

THE SYSTEMATIC SEARCH for a substance capable of blocking the action of histamine began in 1937 in France By 1942 the first

experimental antihistaminic drug that could be used in clinical trial with some measure of safety was synthesized and named Antergan. Between 1942 and 1945 animal experiments were carried out using Neo-Antergan, Benadryl and Pyribenzamine which were relatively nontoxic and safe for clinical use. Since then a host of related substances has been developed.

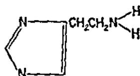
Antihistamines produce their effect by blocking some of the actions of histamine rather than by causing pharmacologic responses which are antagonistic to those induced by histamine. No antihistamine antagonizes all the effects of histamine. And all antihistamines have some physiologic action unrelated to histamine interference.

Indication. The antihistamines are used in urticarial types of hypersensitivity and angioneurotic edema. They may be worth while although their value has not been proved in other allergic reactions and in eczematous eruptions associated with pruritus. They are useful for mild sedation and are beneficial as a mouthwash or spray for painful mucous membrane lesions such as occur in pemphigus and aphthous stomatitis.

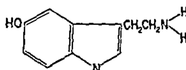
Mechanism of action. It will be noted in the following chart that a side chain $-CH_2CH_2N-$ is common to histamine, serotonin, nor-epinephrine and epinephrine. This side chain also occurs in the antihistamines, antiemetics, anti-motion sickness drugs and some of the tranquilizers. It is likely that because of this common side chain antihistamines can compete with histamine for physiologic receptor sites in the cell and thereby block the response to histamine. Part of the action of epinephrine in combating allergic reactions may be on a similar basis. The antihistamines do not prevent release of histamine or undergo chemical reaction with it.

Since the common side chain also is present in potent physiologic substances other than histamine, it is no wonder that the antihistamines have pharmacologic actions independent of histamine blockage. As tranquilizers they influence serotonin and nor-epinephrine metabolism in the central nervous

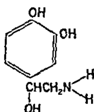
Physiologic Amines



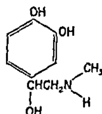
Histamine



Serotonin

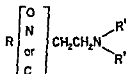


Nor epinephrine



Epinephrine

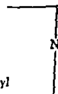
The Three Antihistamine Groups



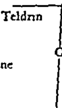
Benadryl
Ambodryl
Decapryn
Dramamine
Diafen



Pyribenzamine
Neo Antergan
Thenfadil
Phenergan
Theruhistin
Pyrrolazote
Thenylene Histadyl
Tagathen



Chlor Trimeton Teldrin
Polaramine
Dimetane
Actidil
Perazil Di Paralene
Bonamine
Thephorin
Pyronil



system They have antiemetic and anti motion sickness properties Topically most antihistamines are local anesthetics The common side chain also is found in substances such as procaine

The $-CH_2CH_2N-$ group is attached to the rest of the molecule through an oxygen nitrogen or carbon atom In some of the antihistamines with a carbon attachment the carbon atom is asymmetric, and the drugs are obtained as DL mixtures In one case (Chlor Trimeton) resolution showed that only the *dextro* form (Polaramine) is active biologically whereas the levo form is inactive

Toxic agents which produce urticaria probably do so by acting upon the mast cells in the dermis which release histamine and heparin in response to injury In some allergic reactions one observes the triple response of Lewis which consists of

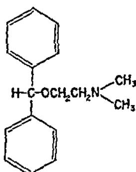
1 Red reaction—due to capillary dilatation
2 Diffuse flare—due to arteriolar dilatation mediated through an axon reflex
3 Wheal or local edema—corresponding to the *previous* site of capillary dilatation resulting from transudation of fluid because of increased capillary permeability

The first and third components of this response result from the release of histamine Antihistamines can block histamine and prevent the development of these effects

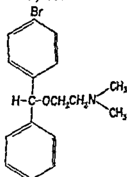
When present as the hydrochloride antihistamines do not penetrate intact skin They are absorbed in damaged skin and may be effective in some cases of pruritus It is possible that some of the antipruritic action resulting from local application of antihistamines is due to inhibition of the cutaneous nerve fibers which mediate the sensations of itch and pain Unfortunately severe epidermal sensitization may result from topical application of antihistaminic drugs For this reason it is wiser to use other antipruritic agents topically

Side effects The most common adverse reactions to the antihistamines are sedation excitement vertigo dryness of the mouth nausea, diarrhea and dermatitis

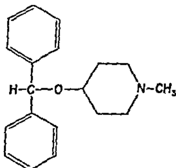
The antihistamines usually are prepared as the hydrochloride maleate,



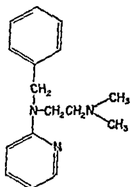
Benadryl
(Diphenhydramine)



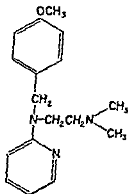
Ambodryl
(Bromodiphenhydramine)



Diafen
(Diphenylpyraline)

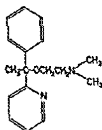


Pyribenzamine
(Tripelennamine)

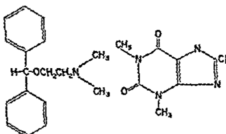


Neo-Antergan
(Pyrilamine)

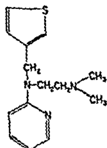
succinate citrate or tartrate However the salt forms are not given in this book



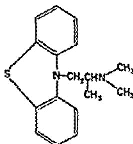
Decapryn
(Doxylamine)



Dramamine
(Dimenhydrinate)

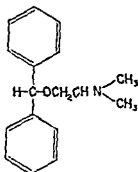


Thenfadil
(Thenyldiamine)

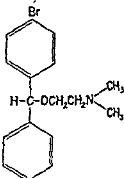


Phenergan
(Promethazine)

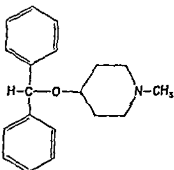
The antihistamines usually are prepared as the hydrochloride maleate,



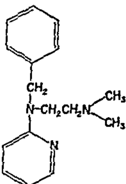
Benadryl
(Diphenhydramine)



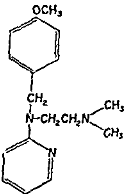
Ambodryl
(Bromodiphenhydramine)



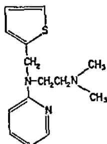
Diafen
(Diphenylpyraline)



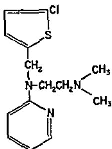
Pyribenzamine
(Tripelennamine)



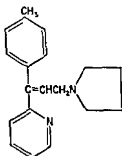
Neo-Antergan
(Pyrilamine)



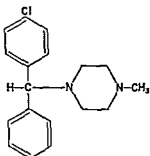
Thenylene Histadyl
(Methapyrilene)



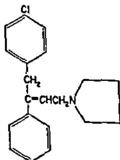
Tagathen
(Chlorothen)



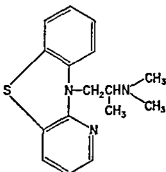
Actidil
(Triprolidine)



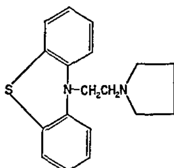
Perazil Di Paralene
(Chlorcyclizine)



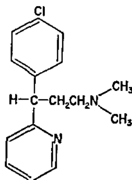
Pyronil
(Pyrrobutamine)



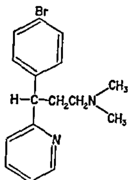
Theruhistin
(Isothipendyl)



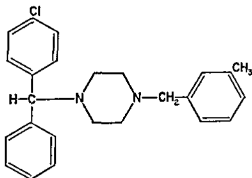
Pyrrolazote
(Pyrathiazine)



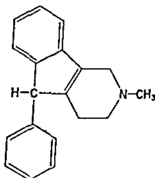
Chlor Trimeton Teldrin
(DL mixtures), Polaramine (D form)
(Chlorpheniramine)



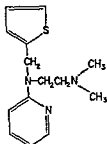
Dimetane
(Parabromdylamine)



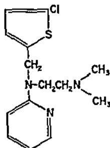
Bonamine
(Meclizine)



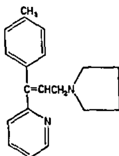
Thephorin
(Phenindamine)



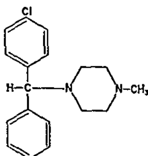
Thenylene Histadyl
(Methapyrilene)



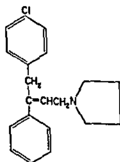
Tagathen
(Chlorothen)



Actidil
(Triprolidine)



Perazil Di Paralene
(Chlorcyclizine)



Pyronil
(Pyrrobutamine)

Antihistamines are available in many forms—tablets, capsules, liquids, suppositories, sustained release preparations, etc. Because individuals react differently to the antihistamines, the drug that is effective in one case may be ineffective in another with regard to either the antihistaminic or the sedative action Consequently, if satisfactory results are not obtained with one antihistamine, another may be tried Sometimes combinations of antihistamines are more effective than comparable doses of one alone The commonly used antihistamines and their oral doses are

ANTIHISTAMINE	ADULTS 3-4 Times Daily*	CHILDREN 1-4 Times Daily	
Benadryl			
25 and 50 mg capsules	50–100 mg	Under 1 yr	5 mg
Elixir 10 mg./4 ml		1–5	10–20 mg
		5–12	20–50 mg
Ambodryl			
25 mg capsules	25–50 mg	Under 1 yr	5 mg
Elixir 10 mg /4 ml		1–5	10–20 mg
		5–12	20–50 mg
Decapryn			
12 5 and 25 mg tablets	12 5–25 mg	Under 1 yr	3 1 mg
Syrup 6 25 mg /5 ml		1–5	6 25 mg
		5–12	6 25–12 5 mg
Dramamine			
50 mg tablets	50 mg	1–5 yr	6 3–12 5 mg
Liquid 12 5 mg./4 ml		5–12	12 5–25 mg
Suppositories 100 mg			
Diafen			
2 mg tablets	2 mg	1–5 yr	1 mg
		5–12	2 mg
Pyribenzamine			
25 and 50 mg tablets	50–100 mg	Under 1 yr	5 mg
Elixir 20 mg /4 ml		1–5	10–20 mg
		5–12	20–50 mg
Neo-Antergan			
25 and 50 mg tablets	25–50 mg	1–5 yr	10 mg
		5–12	25 mg
Thenfadil			
15 mg tablets	15 mg		
Phenergan			
12 5 and 25 mg tablets	12 5 mg 3–4 x daily 25 mg h s		
Theruhistin			
4 mg tablets	4 mg	1–5 yr	1 mg
Syrup 2 mg./5 ml		5–12	1–2 mg
Pyrrolazote			
25 and 50 mg tablets	25–50 mg	5–12 yr	12.5–25 mg

*Unless otherwise specified

ANTIHISTAMINE	ADULTS 3-4 Times Daily	CHILDREN 1-4 Times Daily	
Thenylene Histadyl 50 mg tablets and capsules	50–100 mg		
Tagathen 25 mg tablets	25–50 mg		
Chlor Trimeton, Teldrin 4 mg tablets Syrup 2 mg./5 ml (Teldrin—spansule only)	4 mg	Under 1 yr 1–5 5–12	0 5–1 mg 1–2 mg 2–4 mg
Polaramine 2 mg tablets	2 mg		
Dimetane 4 mg tablets Elixir 2 mg./5 ml	4–8 mg	1–5 yr 5–12	2 mg 2–4 mg
Actidil 2.5 mg tablets Syrup 1 25 mg /5 ml	2.5 mg	Under 1 yr 1–5 5–12	0 6 mg 1 25 mg 1 25–2 5 mg
Perazil Di Paralene 25 and 50 mg tablets	50 mg 1–2 x daily	Under 1 yr 1–5 5–12 1–2 times daily	12.5 mg 12.5–25 mg 1 25–2 5 mg
Bonamine 25 mg tablets or chewing tablets Elixir 12 5 mg /5 ml	25 mg	5–12 yr once daily	12.5–25 mg
Thephorin 10 and 25 mg tablets Syrup 10 mg /5 ml	10–50 mg		
Pyronil 15 mg tablets	15 mg		

EPINEPHRINE FOR ACUTE ALLERGIC REACTIONS

Epinephrine (Adrenalin) is the treatment of choice for acute anaphylactic reactions It is also useful for acute giant hives and laryngeal edema Some of its actions are similar to those of the antihistamines It may prevent urticaria formation by causing vasoconstriction and decreasing vessel permeability so that fluid does not escape into the tissues It is possible that epinephrine may have a slight action in stimulating the pituitary gland to produce adrenocorticotropic hormones

Antihistamines are available in many forms—tablets, capsules, liquids, suppositories, sustained release preparations, etc. Because individuals react differently to the antihistamines, the drug that is effective in one case may be ineffective in another with regard to either the antihistaminic or the sedative action. Consequently, if satisfactory results are not obtained with one antihistamine, another may be tried. Sometimes combinations of antihistamines are more effective than comparable doses of one alone. The commonly used antihistamines and their oral doses are:

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25 and 50 mg. capsules	50–100 mg.	Under 1 yr.	5 mg.
Elixir 10 mg./4 ml.		1–5	10–20 mg.
		5–12	20–50 mg.
Ambodryl			
25 mg. capsules	25–50 mg.	Under 1 yr.	5 mg.
Elixir 10 mg./4 ml.		1–5	10–20 mg.
		5–12	20–50 mg.
Decapryn			
12.5 and 25 mg. tablets	12.5–25 mg.	Under 1 yr.	3.1 mg.
Syrup 6.25 mg./5 ml.		1–5	6.25 mg.
		5–12	6.25–12.5 mg.
Dramamine			
50 mg. tablets	50 mg.	1–5 yr.	6.3–12.5 mg.
Liquid 12.5 mg./4 ml.		5–12	12.5–25 mg.
Suppositories 100 mg.			
Diafen			
2 mg. tablets	2 mg.	1–5 yr.	1 mg.
		5–12	2 mg.
Pyribenzamine			
25 and 50 mg. tablets	50–100 mg.	Under 1 yr.	5 mg.
Elixir 20 mg./4 ml.		1–5	10–20 mg.
		5–12	20–50 mg.
Neo-Antergan			
25 and 50 mg. tablets	25–50 mg.	1–5 yr.	10 mg.
		5–12	25 mg.
Thenfadil			
15 mg. tablets	15 mg.		
Phenergan			
12.5 and 25 mg. tablets	12.5 mg. 3–4 x daily 25 mg. h.s.		
Theruhistin			
4 mg. tablets	4 mg.	1–5 yr.	1 mg.
Syrup 2 mg./5 ml.		5–12	1–2 mg.
Pyrrolazote			
25 and 50 mg. tablets	25–50 mg.	5–12 yr.	12.5–25 mg.

* Unless otherwise specified.

quired Oozing is a contraindication to the use of lotions because caking may occur leading to retention of debris and bacteria Liniments are lotions which contain oil They are unstable emulsions of oil in water which may or may not contain powder and are used in acute nonweeping dermatoses when cooling and protection without excessive drying are required Ointments are semisolids containing oily substances They are used for lubrication and protection as explained in the section Ointment Bases and Lubricating Agents Topical use of steroids for treatment of pruritus is given in the section on Steroids and ACTH

LOTIONS AND LINIMENTS

These preparations are used for the treatment of acute dermatitis especially when pruritus is present and the stage of weeping is over They may be applied to the skin with the finger tips or a soft paint brush 2 to 4 times a day Lotions or liniments should not be put on oozing or crusted lesions since they may occlude the area and promote bacterial growth The following lotions and liniments are available on prescription

Calamine Lotion (suspension)

Calamine	80 Gm
Zinc oxide	80 Gm
Glycerin	20 ml
Bentonite magma	250 ml
Calcium hydroxide solution to make	1 000 ml

Calamine is zinc oxide (ZnO) with 0 5% ferric oxide (Fe_2O_3) for coloring purposes Because of the variable color of calamine the National Formulary previously recognized Prepared Neocalamine which is 93% zinc oxide (ZnO) 3% ferric oxide (Fe_2O_3) and 4% yellow ferric oxide ($2Fe_2O_3 \cdot 3H_2O$) Although neocalamine simulates natural skin color more closely than calamine it is not as useful because it stains clothing Bentonite magma is a form of bentonite used as a suspending and emulsifying agent It is a clay mineral consisting chiefly of aluminum silicates and small amounts of feldspar gypsum

Dose A 1 1,000 solution of Adrenalin in water may be given subcutaneously or intramuscularly as follows
Adults—0 2–0 3 ml Repeat every 2 hours if necessary
Children—0 1 ml /10 kg of body weight Maximum single dose is 0 3 ml
A 1 500 solution in oil may be given to adults in a single dose of 1 ml

Antipruritic Lotions, Liniments and Ointments

UNTIL THE ADVENT of steroids for topical use lotions, liniments and ointments were used in dermatologic treatment because their physical properties made them of therapeutic value The steroids have an almost specific chemical action in the control of eczematous changes and pruritus This chemical effect is often much greater than that afforded by the physical properties of lotions liniments and ointments It is for this reason that in the past few years the steroids have replaced so many of the older topical preparations However, the nonsteroid lotions, liniments and ointments still are useful when it is necessary to cover large parts of the body, when steroids are contraindicated and when it is necessary to have an inert vehicle for a drug

Nowadays lotions are suspensions of powder in water to which a suspending agent, such as methylcellulose, has been added Formerly the suspensions of powder were unstable and the lotions had to be shaken before application—hence the term shake lotions Lotions also contain hygroscopic agents which, by decreasing the rate of evaporation of water from the skin, promote a uniform and continuous rate of evaporation, leading to cooling In addition, after most of the water has evaporated, the remaining powder particles form an adherent protective layer on the skin Lotions are of value in the treatment of acute, nonweeping dermatoses when cooling drying and protective actions are re

quired Oozing is a contraindication to the use of lotions because caking may occur leading to retention of debris and bacteria Liniments are lotions which contain oil They are unstable emul sions of oil in water which may or may not contain powder and are used in acute nonweeping dermatoses when cooling and protection without excessive drying are required Ointments are semisolids containing oily substances They are used for lubrica tion and protection as explained in the section Ointment Bases and Lubricating Agents Topical use of steroids for treatment of pruritus is given in the section on Steroids and ACTH

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Tucks (Fuller)

Tucks are flannel pads impregnated with glycerin and witch hazel They are used as a substitute for toilet tissue in the treatment of anal pruritus

Glycerin	10%
Witch hazel	50%
Distilled water	40%

Witch hazel, a fluid extract of twigs of Hammamelis virginiana contains tannin gallic acid and volatile oil

Available in jars containing 120 pads

OINTMENTS

Ointments are used to combat pruritus and for lubrication after the acute stage of dermatitis has subsided The ointment base occludes the surface of the skin thus reducing loss of water Retention of water results in swelling of the horny layer In addition there may be an increase in permeability so that drugs incorporated in the ointment can penetrate more easily For these reasons ointment bases alone or in conjunction with salicylic acid are useful for the treatment of dry skin pruritus hiemalis (winter itch) or ichthyosis Water washable bases usually retain less water on the skin surface than water in-oil or inert oil bases However the water washable bases are more easily removed from the skin

Substances commonly incorporated into ointments are phenol menthol camphor salicylic acid and tar Phenol acts directly on the free epidermal nerve endings to cause analgesia Menthol acts directly on the cold receptors of the skin to cause a feeling of coolness thus suppressing the sensation of itching Camphor is absorbed through mucous membranes and from subcutaneous tissue When used locally it has an irritant effect and probably a benumbing influence upon the peripheral sensory nerves It acts as a local anesthetic to relieve itching Salicylic acid is keratolytic that is it causes shedding of the horny layer and permits penetration into the skin of other agents incorporated into the ointment. The keratolytic effect is dependent upon the concentration of salicylic acid Tar promotes normal keratinization

beidellite, calcium carbonate, volcanic glass, quartz mica and manganese carbonate. Chemically, it is similar to kaolin, but it differs physically in that the particles are finer, giving more surface area for adsorption. Bentonite has the property of *forming highly viscous suspensions or gels with not less than 10 times its weight of water.* Calcium hydroxide combines with proteins present in serous discharges from the skin to form a protective coating on the surface.

Calamine Liniment (emulsion)

Calamine	80 Gm
Zinc oxide	80 Gm
Olive oil	500 ml
Calcium hydroxide solution to make	1 000 ml

Calamine liniment is a water in oil emulsion containing the same proportion of calamine and zinc oxide represented in the formula for calamine lotion. Because of its oil content, the liniment is less drying than the lotion.

Adjuncts 0.5–1% phenol may be added to enhance antipruritic effect. Even though phenol is absorbed through the skin, most of it is rapidly detoxified. However, large denuded areas should not be exposed to prolonged contact with preparations containing phenol. 0.5–1% salicylic acid may be added for a mildly keratolytic effect. To combat infection, antibiotics may be incorporated, singly or in combination, in the following concentrations: bacitracin 100–200 units/ml or neomycin 2 mg/ml.

Schamberg's Lotion

Menthol	0.25%
Phenol	1.0 %
Peanut oil	45.0 %
Calcium hydroxide solution	45.0 %
Zinc oxide powder	8.0 %

Wise's Shake Lotion

Aluminum acetate	12.5%
Glycerin	20.0%
Talcum powder	25.0%
Zinc oxide	25.0%
Calcium hydroxide solution	17.5%

Chemotherapeutic Drugs

In the past 15 years there has been a great increase in the number of agents available to treat infections Concomitant with this productivity has been a tendency to use chemotherapeutic agents generously sometimes loosely Frequently this has resulted in emergence of resistant organisms and occasionally in 'super infections' such as systemic candidiasis (moniliasis) or staphylococcal enterocolitis In this section will be described commonly used antibiotics Some of them are prepared as special salts which increase gastrointestinal absorption Many are available in mixtures but only the individual drugs will be presented here A few combinations for the treatment of staphylococcal infections will be suggested On occasion for resistant staphylococci one may have to resort to systemic administration of neomycin or bacitracin although usually these drugs are used topically because nephrotoxicity may result from parenteral administration Because of the large number of patients having infections caused by strains of staphylococci resistant to several antibiotics it is most important, when possible to obtain cultures and sensitivity tests of material from the active lesions After the culture material has been obtained antibiotic therapy may be started In two or three days, when results of sensitivity tests are known it can be decided whether the originally prescribed antibiotic should be continued or one or 2 other antibiotics substituted Whenever possible incisional drainage should be carried out

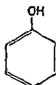
The chemical structures of the various groups of antibiotics differ greatly from one another However one characteristic common to all is that their structures are found in micro-organisms but not in animal tissues Perhaps it is this property that makes chemotherapy possible Thus penicillin is a condensed dipeptide of amino acids of the D configuration Chloramphenicol also is a modified amino acid of the D type In addition it has an aromatic nitro group and a dichloroacetyl group which are not present in

The following ointments, available on prescription, are applied to the involved areas 2 to 4 times daily to relieve pruritus and to keep the skin free from excess surface keratin

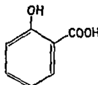
Antipruritic Ointment

Phenol*	0.5–1%
Menthol	0.25 %
Salicylic acid	0.5–1%
Tar (LCD Zetar etc.)	

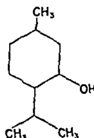
In a water washable base



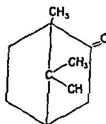
Phenol



Salicylic acid



Menthol



Camphor

Phenol is a distillation product of coal tar, or it may be synthesized from benzene. Menthol is an alcohol obtained from mint oil or prepared synthetically. Camphor is a ketone obtained from the camphor tree, Cinnamomum camphora, an evergreen of eastern Asia, or produced synthetically from fractional distillation of turpentine.

Lubricating Ointment

Salicylic acid	1%

In Nivea, Eucerine or other W/O base

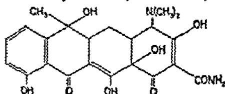
The salicylic acid concentration can be varied from 0.5 to 3%

*Camphor 0.5–1% may be substituted

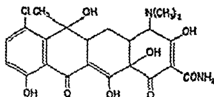
FOR ORAL AND PARENTERAL USE

Tetracyclines

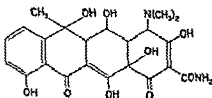
Like most antibiotics, the tetracyclines are derived from fungi of the Actinomycetes family and the Streptomyces genus.



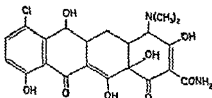
Tetracycline
(Achromycin, Panmycin Polycycline Tetracyn)



Chlortetracycline
(Aureomycin)



Oxytetracycline
(Terramycin)



Demethylchlorotetracycline
(Declomycin)

animal tissues The polypeptide antibiotics, bacitracin, polymyxin, gramicidin and tyrocidine, contain both D and L amino acids Animal cells contain only amino acids of the L series The tetracyclines have a naphthacene ring system that may be considered to consist of modified amino sugars New types of amino sugars also are found in streptomycin, kanamycin, neomycin, novobiocin, erythromycin and oleandomycin

Under each antibiotic the commonly used names of the susceptible micro organisms will be given The common names and their technical counterparts are as follows

GRAM POSITIVE BACTERIA

I *Cocci*
- Staphylococcus (*Micrococcus pyogenes var aureus, albus*)
- Streptococcus (Streptococcus pyogenes beta hemolytic streptococci)
- Pneumococcus (Diplococcus pneumoniae)

II *Bacilli*
- Anthrax (Bacillus anthracis)
- Clostridia (Clostridium perfringens, tetani, etc)
- Diphtheria (Corynebacterium diphtheriae)

GRAM NEGATIVE BACTERIA

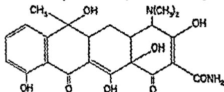
I *Cocci*
- Gonococcus (*Neisseria gonorrhoeae*)
- Meningococcus (Neisseria intracellularis)

II *Bacilli*
- Proteus (Proteus vulgaris)
- Pyocyaneus or Pseudomonas (Pseudomonas aeruginosa)
- E coli (*Escherichia coli*)
- Hemophilus (Hemophilus ducreyi influenzae, etc)
- Brucella (Brucella abortus etc)
- Aerobacter (Aerobacter aerogenes)
- Friedländer s bacillus (Klebsiella pneumoniae)
- Pasturella (Pasturella pestis tularensis)
- Salmonella (Salmonella typhosa etc)
- Shigella (Shigella dysenteriae etc)
- Bacteroides (Bacteroides funduliformis)

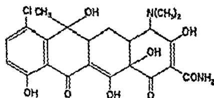
FOR ORAL AND PARENTERAL USE

Tetracyclines

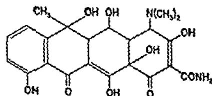
Like most antibiotics the tetracyclines are derived from fungi of the Actinomycetes family and the Streptomyces genus.



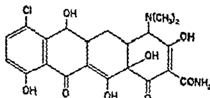
Tetracycline
(Achromycin Panmycin Polycycline Tetracyn)



Chlortetracycline
(Aureomycin)



Oxytetracycline
(Terramycin)



Demethylchlorotetracycline
(Declomycin)

Antibiotic spectrum Gram positive and gram negative bacteria, large viruses such as those causing psittacosis, lymphopathia venereum, etc, rickettsiae, Endamoeba histolytica, bacteroides Tetracycline, chlorotetracycline and oxytetracycline are not effective against proteus and pyocyaneus although some strains of these bacteria may be susceptible to demethylchlorotetracycline

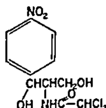
Mode of action Bacteriostatic through interference with microbial protein synthesis or with cellular oxidative metabolism

Dose Adults—250–500 mg 4 times daily orally
Children—25 mg /kg of body weight daily orally
The dose of Declomycin is ½ that given for the other three tetracyclines

Side effects Skin reactions, such as urticaria and pruritic, erythematous, papular eruptions, nausea, vomiting diarrhea, candidiasis

Chloramphenicol (Chloromycetin)

Although chloramphenicol was first obtained from Streptomyces venezuelae, it is now produced synthetically Of the four isomers of chloramphenicol only the natural D threo form is active, and this is the one that is made synthetically It is effectively absorbed from the gastrointestinal tract, and practically none is excreted in the feces



Chloramphenicol
(Chloromycetin)

Antibiotic spectrum Gram positive and gram negative bacteria (especially staphylococci and Salmonella typhosa), large

viruses such as those causing psittacosis lymphopathia venereum etc rickettsiae

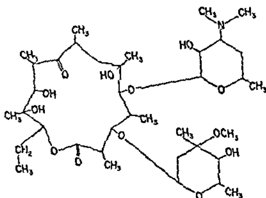
Mode of action Bacteriostatic against staphylococci

Dose Adults—250-500 mg 4 times daily orally
Children—50 mg /kg of body weight daily orally

Side effects Skin reactions such as urticaria nausea vomiting, diarrhea blood dyscrasias sometimes associated with fever

Erythromycin (Erythrocin Ilotycin)

This drug produced by Streptomyces erythreus frequently is used for the treatment of staphylococcal infections especially when the latter are resistant to penicillin and the tetracyclines A useful combination consists of erythromycin and chloramphenicol which together have a synergistic effect against Micrococcus pyogenes var aureus The propionyl ester of erythromycin (Ilosone) may be a more effective form of this drug for oral use



Erythromycin
(Erythrocin Ilotycin)

Antibiotic spectrum Gram positive bacteria (especially staphylococci) gonococcus meningococcus hemophilus large viruses such as those causing psittacosis lymphopathia venereum etc rickettsiae

Mode of action Erythromycin seems to act against multiplying bacteria It is bacteriostatic against staphylococci

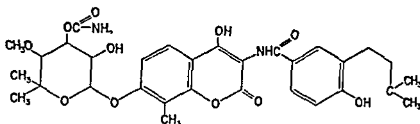
Dose Adults—250–500 mg 4 times daily orally

Children—5 mg /lb of body weight 4 times daily

Side effects Occasionally mild gastrointestinal upsets

Novobiocin (Albamycin, Cathomycin)

This antibiotic, produced by Streptomyces niveus, is used chiefly for infections caused by staphylococci resistant to other antibiotics and for urinary tract infections caused by strains of proteus



Novobiocin
(Albamycin Cathomycin)

Antibiotic spectrum Gram positive bacteria (especially staphylococci), proteus

Mode of action Bacteriostatic May be bactericidal in high concentration

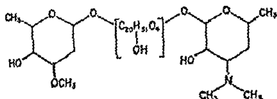
Dose Adults—1 Gm initially followed by 250–500 mg 4 times daily orally

Children—15–45 mg /kg of body weight daily orally

Side effects Reversible leukopenia erythematous, papular and urticarial skin eruptions, fever

Oleandomycin (Matromycin or the triacetyl derivative Cyclamycin Tao)

This antibiotic, isolated from Streptomyces antibioticus is of questionable value in infections caused by staphylococci resistant to other antibiotics



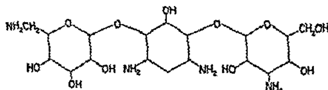
L—OLEANDROSE DESOSAMINE

Oleandomycin
(Matromycin Cyclamycin Tao)

Antibiotic spectrum Gram positive bacteria gonococcus meningococcus brucella Hemophilus influenzae
Mode of action Weakly bactericidal and bacteriostatic.
Dose Adults—250–500 mg 4 times daily orally
Children—30 mg /kg of body weight orally daily

Kanamycin (Kantrex)

This antibiotic isolated from Streptomyces kanamyceticus is structurally similar to neomycin and streptomycin It has the unusual property of being stable indefinitely at room temperature Being a water soluble basic substance which is poorly absorbed from the intestinal tract it is given orally for intestinal infections but must be given intramuscularly when systemic therapy is required It is used for the treatment of infections caused by staphylococci resistant to other antibiotics



Kanamycin
(Kantrex)

Antibiotic spectrum Gram positive and gram negative bacteria (especially staphylococci)
Mode of action Bactericidal
Dose Adults—3–4 Gm orally or 1–2 Gm intramuscularly in equally divided doses daily

Children—50 mg/kg of body weight orally or 15–30 mg/kg intramuscularly in 2 to 4 equally divided doses daily

Side effects Renal irritation evidenced by casts, microscopic hematuria and albuminuria may follow intramuscular administration These signs are reversible Auditory damage sometimes occurs after high and prolonged intramuscular dosage Kanamycin *is contraindicated in intestinal obstruction*

Ristocetin A and B (Spontin)

Ristocetin A and B, antibiotics isolated from the actinomycete, Nocardia lurida, are polysaccharides composed primarily of pentose units Both compounds have molecular weights of about 4,000 and are relatively stable They are amphoteric substances with isoelectric points near pH 8 The acidic properties are due to phenolic groups, and the basic properties are due to amino groups Hydrolysis yields the four sugars glucose, mannose, arabinose and rhamnose and a mixture of amino acids These two classes of substances account for the bulk of the ristocetin molecule The phenolic groups are associated with the amino acids The difference between ristocetin A and B appears to lie primarily in the proportions of the sugars There is more arabinose in ristocetin A than in B In animals, ristocetin B is a more potent antimicrobial agent than A, but it is also more toxic A mixture of approximately 95% ristocetin A and 5% ristocetin B is available under the name of Spontin It is given intravenously for the treatment of infections due to gram positive bacteria, particularly staphylococci

Antibiotic spectrum Gram positive bacteria (especially staphylococci)

Mode of action It is bactericidal in the same concentration that it is bacteriostatic

Dose Spontin must be given intravenously in 5% dextrose in water Total daily dose 25–50 mg/kg of body weight divided into 2 to 3 portions and given at 8–12 hour intervals Each intravenous infusion is given over a 35–40 minute period *For* 250 *mg* Spontin 125 ml of 5% dextrose is used Spontin is irritating if deposited in extravascular tissue.

Side effects Dermatitis fever and reversible leukopenia with a relative neutropenia occur Frequent white cell counts should be done during the period of Spontin therapy

Vancomycin (Vancocin)

This drug isolated from Streptomyces orientalis is used for the treatment of staphylococcal infections, especially those resistant to other antibiotics Vancomycin must be given intravenously because little is absorbed from the gastrointestinal tract and because intramuscular injections are painful The chemical structure of vancomycin is not known This antibiotic has a molecular weight of about 3,300 It contains carboxyl, amino and phenolic groups

Antibiotic spectrum Gram positive bacteria

Mode of action Bactericidal

Dose Adults—500 mg intravenously every 6 hours or 2 Gm daily by continuous infusion A vial containing 500 mg vancomycin is diluted to 100-200 ml with saline or 5% glucose in water This solution is given intravenously over a 20-30 minute period

Side effects Urticaria macular eruptions fever nausea feeling of warmth and generalized tingling have occurred

Penicillin

When various chemicals are added to the culture mediums different penicillin antibiotics are produced by strains of Penicillium notatum and Penicillium chrysogenum Chemically it is possible to classify the penicillins with polypeptide antibiotics because they can be considered derivatives of a condensed dipeptide The chemical structures of seven of the penicillins are given in the diagram where the letter R of the penicillin molecule can be any of the chemical groups to the right of G X V F dihydro F K or O The most widely used form is penicillin G Recently a new type of penicillin (Syncillin Maxipen) has been made by a combination of fermentation and chemical addition 6 amino-penicillanic acid is made by biosynthesis and then an α phenoxyethyl group is added chemically This new penicillin is similar to penicillin V which has an α-phenoxymethyl instead of an α-phenoxyethyl group The

Children—50 mg/kg of body weight orally or 15-30 mg/kg intramuscularly in 2 to 4 equally divided doses daily

Side effects Renal irritation evidenced by casts, microscopic hematuria and albuminuria may follow intramuscular administration These signs are reversible Auditory damage sometimes occurs after high and prolonged intramuscular dosage Kanamycin is contraindicated in intestinal obstruction

Ristocetin A and B (Spontin)

Ristocetin A and B, antibiotics isolated from the actinomycete, Nocardia lurida, are polysaccharides composed primarily of pentose units Both compounds have molecular weights of about 4,000 and are relatively stable They are amphoteric substances with isoelectric points near pH 8 The acidic properties are due to phenolic groups, and the basic properties are due to amino groups Hydrolysis yields the four sugars glucose, mannose, arabinose and rhamnose and a mixture of amino acids These two classes of substances account for the bulk of the ristocetin molecule The phenolic groups are associated with the amino acids The difference between ristocetin A and B appears to lie primarily in the proportions of the sugars There is more arabinose in ristocetin A than in B In animals, ristocetin B is a more potent antimicrobial agent than A, but it is also more toxic A mixture of approximately 95% ristocetin A and 5% ristocetin B is available under the name of Spontin It is given intravenously for the treatment of infections due to gram positive bacteria, particularly staphylococci

Antibiotic spectrum Gram positive bacteria (especially staphylococci)

Mode of action It is bactericidal in the same concentration that it is bacteriostatic

Dose Spontin must be given intravenously in 5% dextrose in water Total daily dose 25-50 mg/kg of body weight divided into 2 to 3 portions and given at 8-12 hour intervals Each intravenous infusion is given over a 35-40 minute period For 250 mg Spontin, 125 ml of 5% dextrose is used Spontin is irritating if deposited in extravascular tissue

Antibiotic spectrum Gram positive bacteria, gonococcus, meningococcus spirochetes, Actinomyces bovis, large viruses such as tho e causing psittacosis lymphopathia venereum etc

Penicillin is the drug of choice in infections due to beta hemolytic streptococci or pneumococci. Because of its inherently low toxicity, penicillin may be given in very high doses for staphylococcal infections

Mechanism of action Penicillin inhibits bacteria during the growth pha_e This action results in part becau_e penicillin prevents synthesis of bacterial cell walls and these walls differ chemically from the outer walls of animal cells The cytoplasm of a gram positive bacterium lies within a fragile membrane which is surrounded by a rigid wall The cytoplasm has high osmotic activity but the cell is prevented from bursting by the strength of the wall The walls of staphylococci contain a large molecule made up of D and L alanine D glutamic acid lysine glycine glucosamine and the N acetyl derivative of an amino sugar 3 0 carboxyethyl hexo amine In the growing—but not the resting—phase penicillin prevents the incorporation of the N acetylamino ugar peptide fragment into new cell wall material Thus penicillin treated bacterial cells grow normally but they soon fail to have enough cell wall to go around The inadequate wall can no longer protect the cytoplasmic membrane and the cell bursts

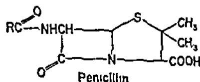
Dose Penicillin has been standardized so that pure crystalline penicillin G contains 1 unit/0 6 μg Hence 1 mg is equivalent to 1 66i units Commercial preparations are required to have a potency of not less than 1 500 μ/mg 600 mg is equivalent to 1 000 000 units

TREATMENT OF SE I INFECTIONS CAUSED BY PENICILL N SENSITIVE ORGANISMS

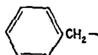
Intramuscular 300 000–600 000 units procaine penicillin daily for 10 days Or 600 000 units long acting benzathine penicillin (Bicillin) once Adequate blood levels will be maintained for 10 days

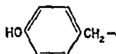
Oral 800 000–1 800 000 units daily in 3 to 4 divided doses

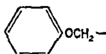
Syncillin penicillin is of special interest because not only is it relatively stable at low pH but also because it has an asymmetric carbon atom The commercial product is a mixture of equal

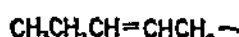


Penicillin type

G 

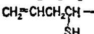
X 

V 

F 

Dihydro F 

K 

O 

parts of the D and L isomers In general the L isomer is 2 to 17 times more active than the D isomer However, the DL mixture usually has the same or greater activity than the L isomer alone

10–15% of most types of penicillin when administered orally, is destroyed by acid in the stomach This loss can be avoided by giving the acid stable, water soluble penicillin V or Syncillin The kidneys excrete penicillin almost as fast as it is absorbed The net effect of orally administered penicillin is estimated to be 1/5 that of the drug given intramuscularly A rule of thumb is that the oral dose should be 4 to 5 times that required for intramuscular injection

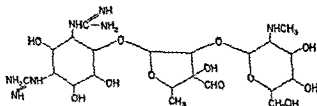
Dose 800 000 units of penicillinase (contents of 1 vial reconstituted with 2 ml of water) intramuscularly is usually sufficient to cause subsidence of the penicillin reaction within 24–48 hours For severe and protracted reactions usually associated with depot preparations a second injection may be needed in 3 to 4 days Steroids and antihistamines should be used concomitantly if necessary Penicillinase does not have time to be effective in acute anaphylactic reactions which cause death within minutes

Side effects Fever, morbilliform eruptions, urticaria local swelling and erythema at site of injection and anaphylactic reactions may occur

Available as Neutrapen (SchenLabs) in single dose vials containing 800 000 units One unit of penicillinase is defined as that amount which would inactivate 1 unit of penicillin per minute.

Streptomycin

Streptomycin is an antibiotic discovered in cultures of the actinomycete Streptomyces griseus Dihydrostreptomycin is obtained by catalytic hydrogenation of streptomycin Its antibacterial spectrum and potency are similar to the parent material but it is more stable evokes fewer hypersensitivity reactions and causes less vertigo but more deafness than streptomycin.



Streptomycin

Antibiotic spectrum Gram negative bacteria Mycobacterium tuberculosis

Mechanism of action Streptomycin combines with nucleic

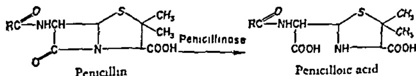
TREATMENT OF SYPHILIS

Primary, secondary, latent and late (all types except neurosyphilis) and syphilis during pregnancy 600 000 units procaine penicillin intramuscularly daily except Saturday and Sunday for 10 injections Total dose, 6,000,000 units For *neurosyphilis increase number of injections to 15 Total dose,* 9,000,000 units

Long acting penicillin (Bicillin) has been tried in single doses of 2 4 or 4 8 *million units The long term efficacy of* this is not known yet

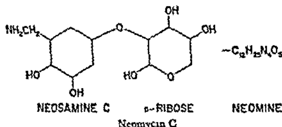
Side effects Different types of allergic reactions occur following administration of penicillin The most common include eczematous eruptions, pruritus, urticaria and exfoliative dermatitis A delayed serum sickness type of sensitization may supervene Anaphylactoid reactions sometimes occur shortly after administration Fatal reactions have been reported The best treatment of acute anaphylactoid reactions is injection of epinephrine Parenteral antihistamines also may be helpful

Treatment of Penicillin Reactions with Penicillinase—Sensitivity reactions to penicillin may be treated with steroids or antihistamines A new type of treatment has been developed using penicillinase, an enzyme that inactivates penicillin Penicillinase is found in B cereus, E coli and many strains of staphylococci Commercial penicillinase is produced from B cereus The enzyme catalyzes the hydrolysis of the lactam ring in penicillin to produce penicilloic acid which has no antibiotic activity and apparently is nonallergenic After exposure to penicillinase, penicillin can no longer elicit a hypersensitivity response In the experimental animal penicillinase acts as an antigenic substance



Penicillin   Penicilloic acid

neomycin A was merely a degradation product of B and it also was found that neomycin B could be separated into two isomeric substances Hence two neomycins are available called neomycin B and neomycin C They are fairly stable compounds and can be used in aqueous solution if desired Chemically parts of the molecule are similar to groupings in streptomycin and kanamycin Neomycins B and C contain the base neamine as half the molecule The other half is made up of D ribose and a diaminohexose—neosamine B or C



Neomycin C

Antibiotic spectrum Gram positive and gram negative bacteria

Side effects Although neomycin is very useful because of its stability and wide range of action it has 2 important disadvantages (1) topical application may result in a contact type sensitization reaction (2) the bacterial flora of the skin particularly when neomycin is applied to body folds and orifices is reduced so much that candidal growth is enhanced and severe candidiasis may result

Bacitracin

The bacitracin antibiotics which are obtained from a strain of Bacillus licheniformis are polypeptides made up of D and L amino acids All contain sulfur The isolation and characterization of the bacitracins have been extremely difficult. The main polypeptide bacitracin A consists of 12 amino acids arranged as shown in the structural formula

A thiazoline ring is present. Bacitracin A probably can exist in tautomeric forms Under certain conditions bacitracin A

acids and nucleoprotein It inhibits the oxidation of ribose nucleic acid and the action of diamine oxidase It is difficult to tell whether these changes are the main ones responsible for the action of streptomycin

TOPICAL ANTIBIOTICS

Several of the antibiotics already discussed are available for topical use, e g, the tetracyclines, erythromycin and chloramphenicol Others, such as penicillin and streptomycin, are too sensitizing to be of value topically In this section neomycin, bacitracin, polymyxin and gramicidin will be described These substances have the advantage of not ordinarily being used systemically, so that the chances of unnecessarily sensitizing a patient to an antibiotic that he may require at a later date are reduced In general, preparations containing combinations of these antibiotics, such as Neosporin, Spectrocin and Neo-Polycin, are of greatest effectiveness Chemotherapeutic agents which are not antibiotics are available, such as Vioform Sterosan and Furacin These substances often are not as effective as the antibiotics or, as in the case of Furacin, are more sensitizing

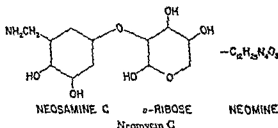
In this section only three commercially available antibiotic ointments and lotions are listed Many others are available These preparations are effective against gram positive and gram negative organisms and are particularly useful for the treatment of staphylococcal infections They should be applied to the skin 2 to 3 times daily In some cases of recurrent staphylococcal infections of the skin it is advisable to apply the antibiotic to the nasal mucous membranes twice daily for 2 weeks in order to eliminate transfer of infection from the nose to the skin via the hands

Neomycin

Neomycin, an antibiotic obtained from Streptomyces fradiae, is active against a wide range of gram positive and gram negative bacteria as well as Mycobacterium tuberculosis

Several years ago *crude neomycin was separated into 2* products, neomycin A and B Subsequently it was found that

neomycin A was merely a degradation product of B and it also was found that neomycin B could be separated into two isomeric substances Hence two neomycins are available, called neomycin B and neomycin C They are fairly stable compounds and can be used in aqueous solution if desired Chemically parts of the molecule are similar to groupings in streptomycin and kanamycin Neomycins B and C contain the base neamine as half the molecule The other half is made up of D ribose and a diaminohexose—neosamine B or C



Neomycin C

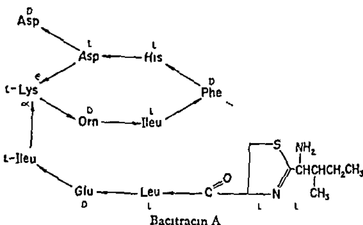
Antibiotic spectrum Gram positive and gram negative bacteria

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Bacitracin

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A thiazoline ring is present Bacitracin A probably can exist in tautomeric forms Under certain conditions bacitracin A



Bacitracin A

can be transformed through internal rearrangement and the loss of ammonia into bacitracin F Bacitracin B is less stable and appears in smaller quantities than bacitracin A It contains all the amino acids present in A plus valine Bacitracin B can exist in at least 2 different forms on the basis of rearrangement of some of the amino acids present

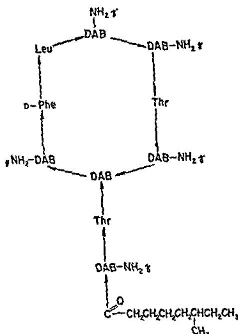
Antibiotic spectrum Gram positive bacteria Inactive against gram negative bacteria except gonococcus and meningococcus

Mode of action The antibiotic activity and mechanism of action of the bacitracins are similar to those of the penicillins

Polymyxin

The polymyxins are antibiotics formed by different but closely related strains of Bacillus polymyxa All the polymyxins, A, B, C, D and E, are basic cyclic peptides containing α, γ diaminobutyric acid and a fatty acid The antibiotics polypeptin and circulin belong to the polymyxin group Polymyxin B can be separated into polymyxin B_1 and B_2 Polymyxin B_1 contains isopelargonic acid, which is present in all the polymyxins except B_2 and polypeptin B_2 contains an acid which is similar but which has one less carbon atom The preparation used commercially is polymyxin B sulfate

Antibiotic spectrum Gram negative bacteria, including pyocyaneus but not proteus



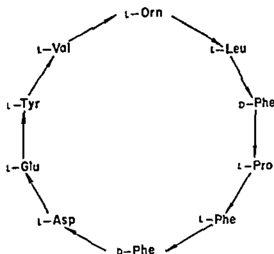
Polymyxin B

DAB = α γ diaminobutyric acid All the amino acids except phenylalanine are in the L form

Tyrothricin Gramicidin and Tyrocidine

Tyrothricin isolated from Bacillus brevis can be separated into 2 groups of polypeptides gramicidin and tyrocidine Gramicidin represents about 10-20% of the mixture and is in turn made up of at least 4 different closely related peptides The 3 major ones are called gramicidin A, B and C The complete structures of the gramicidins have not been worked out. They are cyclic peptides made up of 30-40 amino acid residues B differs from A by the replacement of 2 tryptophane residues with phenylalanine C contains at least one tyrosine but this amino acid is not present in A and B

The tyrocidine group has been resolved into the individual peptides A, B and C Tyrocidine A is made up of 10 amino acids in a cyclic arrangement as shown in the diagram Tyrocidine B differs from tyrocidine A in that the L phenylalanine residue between L proline and D phenylalanine is replaced by L-tryptophane Gramicidin S belongs to the tyrocidine class and can be separated into at least 4 different peptides The major peptide, gramicidin S A, contains 10 amino acids in a ring arrangement with a repeating pentapeptide This pentapeptide has the same sequence as half of the tyrocidine molecule



Tyrocidine A

Antibiotic spectrum Gram positive bacteria

Neosporin (Burroughs Wellcome)

OINTMENT

Each gram contains

Polymyxin B sulfate	5 000 units
Zinc bacitracin	400 units
Neomycin sulfate	3 5 mg (as base)

Standardization

1 mg polymyxin B sulfate contains 10 000 units
1 mg bacitracin A contains 70–80 units

Available in 15 and 30 Gm tubes

LOTION

Each milliliter contains

Polymyxin B sulfate	10 000 units
Neomycin sulfate	3 5 mg (as base)
In a water washable base	

Available in 20 ml plastic bottles

Spectrocin (Squibb)

Each gram of ointment or milliliter of lotion contains

Gramicid n	0 25 mg
Neomycin sulfate	2 5 mg (as base)

Available in 15 and 30 Gm tubes of ointment and 15 ml bottles of lotion

Neo-Polycin (Pitman Moore)

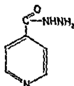
Each gram of ointment contains

Polymyxin B sulfate	8 000 units
Zinc bacitracin	400 units
Neomycin	3 mg (as base)

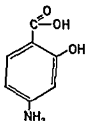
Available in 15 Gm tubes

TUBERCULOSIS OF THE SKIN

Four drugs are used in the treatment of tuberculosis isoniazid, para aminosalicylic acid (PAS) streptomycin and dihydrostreptomycin Usually some combination of these drugs is given Streptomycin has been discussed previously (p 49)



Isonicotinic acid hydrazide
(Isoniazid—Nydrazid Squibb Rimifon Roche)



Para aminosalicylic acid
(PAS)

Mechanism of action Isoniazid acts specifically against the tubercle bacillus and is sometimes effective against Mycobacterium lepraemurium It is inactive against other microorganisms The tubercle bacillus loses its acid fastness when exposed to isoniazid Isoniazid also delays the emergence of resistant organisms Ordinarily this drug is bacteriostatic but it can be given in sufficient concentrations to be bactericidal With isoniazid there is resolution of tubercles with minimal histiocytic activity

PAS inhibits the growth of tubercle bacilli but has little or no effect on other bacteria PAS is not used by itself but in conjunction with streptomycin and/or isoniazid In combination PAS delays emergence of resistant strains of tubercle bacilli

Dose Isoniazid alone—100 mg 3 times daily

Streptomycin with isoniazid—streptomycin 1 Gm intramuscularly twice weekly, isoniazid 100 mg 3 times daily

PAS with isoniazid—PAS 4 Gm 3 times daily at meal time, isoniazid 100 mg 3 times daily

Side effects Isoniazid—constipation difficulty in starting micturition, orthostatic hypotension, eosinophilia, anemia, albuminuria

PAS—dermatitis and local irritation of the gastrointestinal tract consisting of anorexia, nausea, vomiting and diarrhea

Available as isoniazid tablets 50 and 100 mg each and syrup 10 mg /ml PAS available in 0 5 Gm tablets or capsules as the acid or as the calcium or sodium salt and in powder form

SULFONAMIDES

The sulfonamides are of limited u e in infections of the skin due to gram positive bacteria and gram negative cocci Some physicians use them for the treatment of acne vulgaris It must be pointed out that when the sulfonamides are given ultraviolet light therapy must be restricted because of the possibility of photosensitization reactions The sulfonamides also are used for lymphopathia venereum trachoma and inclusion blennorrhea Sulfapyridine has been recommended for the treatment of dermatitis herpetiformis All the sulfonamides without exception can produce dermatitis as a result of a hypersensitivity reaction

1 Triple Sulfonamides
 Mixed sulfonamides are more soluble than single ones because each sulfonamide has a solubility independent of the others present thus decreasing the possibility of precipitation of any of these drugs in the kidney

 Tricombisul (Schering) contains in each 0 5 Gm tablet or each 4 ml of liquid 0 167 Gm each of sulfacetamide, sulfadiazine and sulfamerazine

 Terfonyl (Squibb) contains in each 0 5 Gm tablet or 5 ml of suspension 0 167 Gm each of sulfamethazine sulfadiazine and sulfamerazine

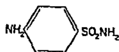
 Tresamide (Merck) contains in each 0 5 Gm tablet 0 1 Gm of sulfamerazine 0 2 Gm of sulfadiazine and 0 2 Gm of sulfathiazole

 Other triple sulfonamide preparations also are available

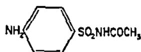
2 Gantrisin (Roche) is highly soluble in neutral and acid solutions

3 Kynex (Lederle) is highly soluble and yet is excreted slowly by the kidney For this reason a daily maintenance dose of 0 5 Gm is all that is necessary In approximately 15% of patients receiving Kynex dermatitis develops Drug fever leukopenia and hepatitis may occur

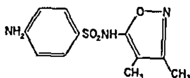
4 Sulfapyridine is not highly soluble in the urine To avoid precipitation of sulfonamide crystals in the renal tubules 1 0 Gm of sodium bicarbonate should be given together with 1 glass of water with each 1 0 Gm of sulfapyridine



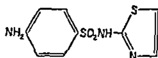
Sulfanilamide



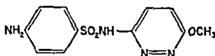
Sulfacetamide



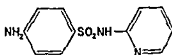
Gantrisin



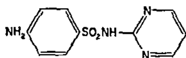
Sulfathiazole



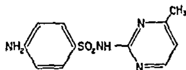
Kynex



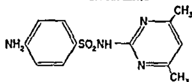
Sulfapyridine



Sulfadiazine



Sulfamerazine



Sulfamethazine

Mechanism of action In general, bacteriostatic but may be bactericidal when present in high concentrations Sulfonamides act partly by displacing para aminobenzoic acid required for growth of bacteria It is possible that in some skin disorders the therapeutic effect of sulfonamides results from a direct metabolic action rather than an antimicrobial

one For example sulfapyridine benefits some patients with dermatitis herpetiformis yet this disease has not been shown to be of infectious etiology

Dose Adults—1 Gm (2 tablets) by mouth 4 to 6 times daily
The dose of Kynex is 0.5 Gm once daily
Children—60 mg/lb of body weight per 24 hours divided into 4 to 6 oral doses

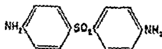
Side effects A variety of dermatologic eruptions—eczematous dermatitis urticaria fixed drug eruptions photosensitization etc—and many systemic side effects such as fever, renal and hepatic toxicity etc may occur

Available in 0 5 Gm tablets

SULFONES

The sulfones are related chemically to the sulfa drugs In general they are more effective than the sulfa drugs both in vitro and in vivo However their greater toxicity limits their clinical usefulness. The sulfones are used primarily in the treatment of leprosy They also are used in dermatology to treat dermatitis herpetiformis and subcorneal pustular dermatosis Since most of the sulfones are metabolized to the parent compound diaminodiphenylsulfone and since this compound is less toxic than the others it is the only one that will be considered

Avlosulfon (Ayerst)



Avlosulfon
(Dapsone DDS 4-4 Diaminodiphenylsulfone)

Dose 50 to 150 mg daily according to the severity of symptoms and response of the patient If medication is continued for several months or years it should be given for 6 days each week allowing 1 day's rest

Available in 100 mg tablets

Side effects Early transient side effects are cyanosis, pallor, methemoglobinemia or sulfhemoglobinemia They are not an indication for withdrawal of the drug unless associated with symptoms of anoxemia Nausea, vomiting, headache, giddiness, tachycardia, psychosis, anemia, fever and exfoliative dermatitis may occur Suppression of the white blood cell count rarely happens, but it is necessary to do white cell counts at regular intervals

Cosmetics

Hypoallergenic Cosmetics

Many people are allergic to powder, rouge, lipstick, cream, etc Cosmetics which contain a minimal amount of allergenic substances are produced by the following companies *Almay*, Ar-Ex, Marcelle, Texas Pharmacal Some of these companies will supply a testing kit to help identify a cosmetic ingredient that may be causing a contact dermatitis In addition they will prepare for individual needs special cosmetics minus the offending agent

Opaque Covering

Tinted, opaque cosmetics are needed to cover disfiguring lesions such as hemangiomas, scars and pigmentary defects One company, Lydia O'Leary, manufactures a variety of agents of this type under the names of Covermark and Spotstik

Enzymic Debridement

PROTEOLYTIC ENZYMES can be used to debride surfaces covered with necrotic tissue and pyogenic membranes as in chronic skin

ulcers burns with eschar formation, infected wounds abscesses, etc The effectiveness of enzymic debridement depends upon the destruction and removal of necrotic tissue at a more rapid rate than removal of normal viable tissue Different enzyme preparations are available in solutions and in ointments The enzymes are trypsin chymotrypsin papain streptokinase and streptodornase

Trypsin catalyzes hydrolysis of peptide bonds after the basic amino acids lysine arginine and histidine Chymotrypsin catalyzes hydrolysis of peptide bonds after the aromatic amino acids phenylalanine tyrosine and tryptophan Papain catalyzes the cleavage of peptide bonds in a relatively nonspecific manner Streptokinase activates the factor present in plasma which causes fibrinolysis Streptodornase causes the breakdown of desoxyribonucleoprotein present in purulent exudates

Solutions containing enzymes should be made up just before use since they are stable for only a few hours at room temperature

Tryptar (Armour)

Tryptar is the purified crystalline enzyme trypsin derived from mammalian pancreas Tryptar loses 75% of its activity in 3 hours in solution at room temperature and hence must be freshly prepared at maximum intervals of 3 hours The potency of the enzyme powder is reduced even more rapidly in the presence of exuding serum The lesion should be exposed to the enzyme until clearance of necrotic debris is accomplished

Application (1) When the lesion is moist sprinkle on dry powder and allow powder to remain for 30 minutes Then wash off and mechanically debride loosened matter Repeat several times daily until all necrotic tissue disappears and clean surface remains

(2) When the lesion is dry, apply sterile gauze sponges moistened with Tryptar solution which has been prepared immediately before use by dissolving Tryptar powder in 15–25 ml water or saline

Available in 10 20 and 30 ml vials containing 50 000 125 000 and 250 000 units respectively

Tryptar Ointment (Armour)

Each gram of this preparation contains

Trypsin	5 000 units
Chymotrypsin	5 000 units
Polymyxin	5 000 units
Bacitracin	500 units

In an ointment base

Tryptar ointment combines proteolytic and antibacterial actions.
Available in 15 Gm tubes

Varidase (Lederle)

Varidase is an enzymic mixture of streptokinase the fibrinolytic principle, and streptodornase, the factor which liquefies purulent exudates, obtained from streptococci Streptokinase is an enzyme activator with maximum activity at pH 7 3-7 6 Streptodornase, a desoxyribonuclease, consists of a series of closely related enzymes

Application Apply sterile gauze sponges moistened with Varidase solution, to lesion Reapply every 24 hours until desired effect is obtained

Available for topical use in vials containing 100,000 units streptokinase together with 25 000 units streptodornase

Varidase Jelly (Lederle)

Mix (1) one 125,000 unit vial of Varidase dissolved in 5 ml sterile water, (2) 15 ml of carboxymethylcellulose jelly Final volume is 20 ml with 5 000 units streptokinase and 1,250 units streptodornase per ml

Application Apply jelly directly to the affected area and keep in situ with gauze or plastic bandages Apply daily or more frequently but allow sufficient intervals to elapse between treatments to permit adequate enzymic action

Available as a set containing 1 vial of Varidase and a 15 ml jar of 4 5% carboxymethylcellulose jelly

Panafil Ointment (Ryston)

Papain powder	10%
Urea	10%
Chlorophyll	0 5%

In a hydrophilic base

Panain is a proteolytic enzyme obtained from papaya the fruit of the papaw or melon tree Carica papaya It is used commercially in the preparation of tenderized meat.

Application Apply directly to lesion and cover with gauze Change dressing once or twice daily Irrigate lesion with saline when redressing in order to remove debris

Available in 1 oz and 4 oz tubes

Fungicidal and Fungistatic Agents

TREATMENT OF FUNGUS INFECTIONS is becoming increasingly hopeful with the advent of new agents for oral and parenteral use in addition to topical preparations Antibiotics for treatment of specific groups of fungi are available for example amphotericin B nystatin and griseofulvin

TOPICAL AGENTS

If the infection is acute wet dressings should be used initially Ointments or liquids are applied to involved areas at bed time and upon arising in the morning For low grade infections in which a moderate amount of perspiration is present powder may be used during the day

OINTMENTS

Sulfur sal thymol ointment Salundek Tricholysin and triacetin preparations are fungistatic and fungicidal in vitro against the trichophyton epidermophyton and microsporon groups of fungi With the exception of triacetin these same agents as well as Nystatin Propion Gel and Gentia Jel act against Candida albicans (monilia) Vioform and Sterosan are useful to treat candidiasis (moniliasis) and mixed infections of fungi and gram positive bacteria Many of these products

are available in combination with steroids and/or antibacterial antibiotics, such as neomycin

To obtain good clinical results it is necessary for the therapeutic agent to reach the fungus This is often difficult when only topical agents are used to treat fungus infections of the scalp and nails The ideal treatment for many of these infections is the use of an oral antifungal substance that may be incorporated into keratin as it is being formed

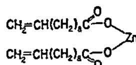
Sulfur Sal Thymol Ointment

Sulfur	2–5%
Salicylic acid	1–3%
Thymol	0.5–2%

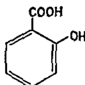
In Desenex ointment



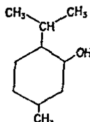
Undecylenic acid



Zinc undecylenate



Salicylic acid



Thymol

Desenex ointment contains 5% undecylenic acid 20% zinc undecylenate and 75% polyethylene glycol

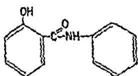
Available Must be prepared on prescription

Salundek Ointment (Maltbie)

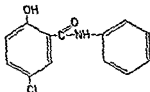
Salicylanilide	3%
Mono- and dichlorosalicylanilides	4%
Undecylenic acid	2%
Zinc undecylenate	10%

In a Carbowax base with a wetting agent

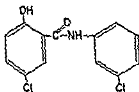
The 4% chlorosalicylanilides consist of 2% 5-chlorosalicyl anilide 1% 5 3' dichlorosalicylanilide and 1% 5 4 dichlorosalicylamide



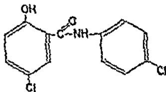
Salicylanilide



5 Chlorosalicylanilide



3 3 Dichlorosalicylanilide

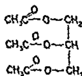


5 4 Dichlorosalicylanilide

Available in 2 oz tubes

Triacetin (Enzactin Ayerst Fungacetin Harvey)

Glyceryl triacetat 25%
In a water washable base



Triacetin
(Glyceryl triacetate)

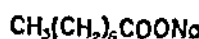
In the presence of esterases enzymes that occur in fungi skin and serum triacetin is hydrolyzed to glycerin and acetic acid The acetic acid liberated at the site of the fungus inhibits its growth Esterases that can catalyze the hydrolysis of triacetin are not present in Candida albicans
Available in 1 oz tubes.

Tricholysin (Kelgy)

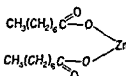
Zinc caprylate	5 %
Sodium caprylate	10 2%
Caprylic acid	1 2%
Normal propyl alcohol	10 %
In a water washable base	



Caprylic acid



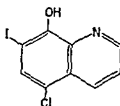
Sodium caprylate



Zinc caprylate

Available in 1 and 8 oz tubes

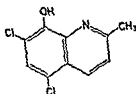
Vioform (Ciba)



Vioform
(5 Chloro 7 iodo-8 hydroxyquinoline)

Vioform is available as 3% iodochlorohydroxyquinoline in a petrolatum base with added Span 80 and in a water washable base made up of sodium lauryl sulfonate, stearyl alcohol spermaceti, glycerin and petrolatum
Available in 50 Gm tubes of ointment or cream

Sterosan (Geigy)



Sterosan
(5 7 Dichloro-8-hydroxyquinaldine)

Sterosan is available as 3% 5 7-dichloro-8 hydroxyquinaldine in an ointment or vanishing cream base
Available in 30 Gm. tubes of ointment or cream

Nystatin (Mycostatin Squibb)

Nystatin sold commercially as Myco tatin is the first effective antifungal antibiotic Its antifungal properties were described in 1950 Nystatin is derived from a species of the actinomycete Streptomyces noursei, which was found in soil from a dairy farm in Virginia owned by a Mr Norris In vitro it is effective against the following fungi candida cryptococcus blastomyces histoplasma and epidermophyton It is somewhat less effective against Microsporum audouini M canis and Trichophyton tonsurans It has no antibacterial action

Nystatin is a water insoluble substance It is a fairly large molecule composed of 40 carbon atoms It has carboxyl lactone and 11 hydroxyl groups and is bound through a glycoside linkage to a 6 carbon amino sugar unit It is susceptible to inactivation by acidic or alkaline reag nts oxidation by air and decomposition by heat and light Chemically, nystatin appears to be related to amphotericin A and B

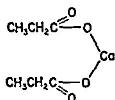
Available as Myco tatin ointment and cream 100 000 units/Gm in 15 and 30 Gm tubes For vaginal infection suppositories containing 100 000 units Mycostatin and 0 93 Gm

lactose per tablet are available in packages of 15 tablets with vaginal applicator

Propion Gel (Wyeth)

Calcium propionate	10%
Sodium propionate	10%

In a water soluble base containing glycerin, 3% boric acid and tragacanth





Calcium propionate   Sodium propionate

Application Introduce ointment into vagina every morning and night for 3 weeks Apply small amount to external genitalia

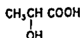
Available in 95 Gm tubes with or without applicator

Gentia-Jel (Westwood)

Gentian violet	0 1%
Acetic acid	1 %
Lactic acid	3 %

In a water soluble polyethylene glycol base





Acetic acid   Lactic acid

Application Insert jelly into vagina at bedtime nightly for 12 nights

Available in packages of 12 single dose prefilled disposable applicators

SOLUTIONS

Verdefam (Texas Pharmacal)

Sodium caprylate	2 %
Sodium propionate	2 %
Propionic acid	3 %
Undecylenic acid	5 %
Salicylic acid	5 %
Copper undecylenate	0.5%
Sodium dioctylsulfosuccinate	0 1%

In water and isopropyl alcohol

Available in 2 oz bottles.

Salundek Solution (Maltbie)

Salicylanilide	3%
Mono- and dichlorosalicylanilides	2%
Undecylenic acid	2%
Ethyl alcohol	55%

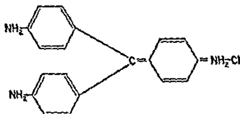
Available in 3 oz bottles

Carfusin (Rorer)

This is carbol fuchsin or Castellani s paint.

Boric acid	1 %
Carbolic acid (phenol)	4 5%
Resorcinol	10 %
Fuchsin	0 3%
Acetone	5 %

In water



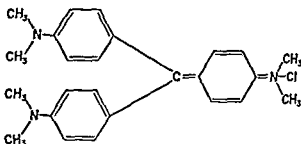
Fuchsin

Basic fuchsin or basic magenta is a mixture of rosaniline and pararosaniline hydrochlorides

Available in 1 and 4 oz. bottles with applicator top

Gentian Violet

Gentian violet is used in a concentration of 0 5–2% in water or 70% alcohol



Gentian violet
(Methylrosaniline chloride methyl violet crystal violet)

Available Must be prepared on prescription

Caution *Avoid staining clothing or other materials* To remove linen stains, wash with sodium carbonate and soap or alcohol.

Onychophytex (Wynlit)

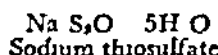
Borotannic complex	7.5%
Salicylic acid	0 8%
Ethyl alcohol	56 %
Ethyl acetate (not specified)	

Borotannic complex is a condensation product made up of 29 parts of boric acid and 46 parts of tannic acid

This preparation has been used for fungus infections of the nails especially those caused by members of the trichophyton group *Its value has not been proved*

Sodium Thiosulfate (sodium hyposulfite)

This is an aqueous solution containing 20% sodium thiosulfate which is used for treatment of tinea versicolor



$Na_2S_2O_3 \cdot 5H_2O$
Sodium thiosulfate

Application Apply to involved areas twice daily Continue treatment for 2 to 3 months following disappearance of lesions to prevent recrudescence

Available Must be prepared on prescription

POWDERS

Desenex (Maltbie)

Undecylenic acid	2%
Zinc undecylenate	20%
Talc	78%

Available in 1½ oz containers

Mycostatin Dusting Powder (Squibb)

This powder contains 100 000 units of nystatin/Gm of talc base.
Available in ½ oz containers

Enzactin Powder (Ayerst)

This preparation contains 33⅓% glyceryl triacetate in a moisture absorbent base
Available in 1½ oz containers

SYSTEMIC AGENTS

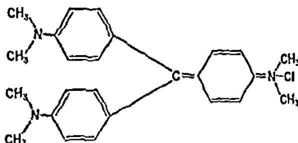
Amphotericin B (Fungizone Squibb)

Amphotericin is a crystalline product obtained from a heretofore unidentified species of streptomyces found in South America Two fractions amphotericin A and B may be separated on the basis of differing solubilities Their chemical structure is still unknown Amphotericin A is related chemically to nystatin Amphotericin B is at present better developed it is more toxic to animals but its in vivo antifungal action is greater than that of amphotericin A despite evidence to the contrary in vitro The in vitro antifungal spectrum of amphotericin A and B includes Candida albicans Cryptococcus neoformans Blastomyces dermatitidis Blastomyces brasiliensis, Sporotrichum schenckii and Histoplasma capsulatum. No antibacterial activity has been observed

Amphotericin B is highly insoluble and is not absorbed through the gastrointestinal tract A water soluble derivative

Gentian Violet

Gentian violet is used in a concentration of 0 5–2% in water or 70% alcohol



Gentian violet
(Methylrosaniline chloride, methyl violet, crystal violet)

Available Must be prepared on prescription
Caution Avoid staining clothing or other materials To remove linen stains, wash with sodium carbonate and soap or alcohol

Onychophytex (Wynlit)

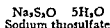
Borotannic complex	7 5%
Salicylic acid	0 8%
Ethyl alcohol	56 %
Ethyl acetate (not specified)	

Borotannic complex is a condensation product made up of 29 parts of boric acid and 46 parts of tannic acid

This preparation has been used for fungus infections of the nails, especially those caused by members of the trichophyton group Its value has not been proved

Sodium Thiosulfate (sodium hyposulfite)

This is an aqueous solution containing 20% sodium thiosulfate which is used for treatment of tinea versicolor



$Na_2S_2O_3 \cdot 5H_2O$
Sodium thiosulfate

Application Apply to involved areas twice daily Continue treatment for 2 to 3 months following disappearance of lesions to prevent recrudescence
Available Must be prepared on prescription

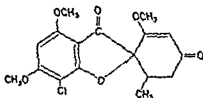
Oral Mycostatin therapy is used for intestinal candidiasis (moniliasis) and for severe candidiasis of the perineum in order to prevent reinfection from the intestinal tract. Mycostatin is highly insoluble Because little is absorbed from the gastrointestinal tract oral Mycostatin is of doubtful value for systemic candidiasis No toxic effects are known

Dose 1 tablet 3 times daily

Available in bottles of 12 and 100 tablets each tablet containing 500 000 units of nystatin, and as a suspension for infants each cubic centimeter containing 100,000 units

Griseofulvin (Grifulvin McNeil Fulvicin Schering)

Griseofulvin is an antibiotic derived from various species of penicillium e g P griseofulvin P palutum P janczewski and P raistrickii Smith Griseofulvin has been called the curling factor because the hyphae of fungi exposed to this material were found to have a characteristic spiral shape as well as a stunting of growth with increased branching abnormal swelling and distortion It seems that griseofulvin becomes attached to keratin as it is formed in skin hair and nails The actual presence of griseofulvin in the developing keratin structures prevents the growth of fungi.



Griseofulvin

In vitro griseofulvin inhibits the growth of a wide variety of fungi It is ineffective against some yeasts In vivo it is effective against microsporon and trichophyton infections of the skin scalp and nails including M canis M audouini M gypseum T rubrum T mentogrophytes T verrucosum T tonsurans etc It is not effective against Candida albicans

is made by combining amphotericin B with a bile salt (desoxycholate), and full antifungal activity is retained The bile salt derivative is prepared commercially for intravenous infusion However, the material also may be dissolved in water and used as a mouth wash It should not be swallowed for systemic treatment because this water soluble amphotericin is not absorbed in the gastrointestinal tract in sufficient quantities to give therapeutic blood levels

Dose Initially, 0 25 mg /kg of body weight daily Gradually increase to 0 75 mg /kg If possible the dose may be increased to 1 0 mg /kg Infusions must be given slowly over a 6 hour period daily or every other day for 2 to 3 weeks or until toxic reactions necessitate temporary cessation of the drug

To prepare the intravenous solution, 10 ml of 5% dextrose in water is added to the vial to make a solution containing 5 mg of amphotericin B/ml Saline or glucose in saline cannot be used because a precipitate forms The quantity needed to give a dose of 0 25 mg /kg of body weight is withdrawn and placed in a container with 200–500 ml of 5% dextrose in water This solution is given over a 6 hour period During the first several days of therapy it is common for chills and fever to occur during the infusion This reaction often can be avoided by giving the patient 10 gr of aspirin when the infusion is begun and again in the middle of the infusion If possible infusions are given at least 5 days a week and the dose increased every other day until an amount equivalent to 0 75 mg /kg is reached This is the usual maintenance dose Patients often require repeated courses of therapy

Side effects In addition to fever there may be back pain in the renal area, rising nonprotein nitrogen levels, headache nausea and vomiting

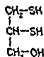
Available in vials containing 50 mg of amphotericin B activity

Mycostatin Oral Tablets (Squibb)

See Mycostatin ointment for description

Heavy Metal Antagonist

THE MOST EFFECTIVE DRUG for treating toxicity due to the heavy metals arsenic gold silver mercury and bismuth is BAL (British anti lewisite) BAL also may be of use in decreasing the hyper pigmentation seen in heavy metal intoxication This drug is contraindicated in cadmium poisoning



BAL (British anti lewisite)
(2 3 Dithiopropanol)

Mode of action BAL combines through sulfhydryl linkages with a heavy metal such as arsenic and the BAL-arsenic complex is excreted in the urine BAL is not used to combat cadmium intoxication because the BAL-cadmium complex formed is nephrotoxic

Dose For intramuscular use only 0 025 ml of ampule solution per kg of body weight is given every 4 hours for 4 to 6 injections for the first 2 days Thereafter the dose is reduced to 2 injections daily for a total of 10 days or until recovery The patient should be informed that BAL is very odorous Side effects such as nausea and sweating may occur If BAL inadvertently enters the blood stream epinephrine or ephedrine should be given subcutaneously immediately to counteract an acute reaction consisting of constriction of the throat and chest etc.

Available in ampules each containing 4 5 ml of 10% solution of BAL in peanut oil with 20% benzyl benzoate (Hynson Westcott & Dunning)

(candidiasis), Malassezia *furfur* (*tinea versicolor*) and Blastomyces dermatitidis (blastomycosis)

Dose *Trichophyton infections* 1 Gm daily in either a single or divided dose for 4 weeks After 4 weeks the dose may be reduced to 0 5 Gm daily for an additional 4 to 8 weeks *Microsporon infections in children* Two possible schedules are

(1) 2 to 3 Gm in a single dose This dose may be repeated once 3 weeks later When possible the hairs should be clipped short 3 weeks after onset of therapy

(2) 250 mg daily for 4 weeks

Available in 250 mg tablets

Side effects Morbilliform or papular eruptions, gastrointestinal disturbances headache, serum sickness, albuminuria and leukopenia have been reported

Iodides

KI	NaI
Potassium iodide	Sodium iodide

Indication Sporotrichosis

Dose Either potassium iodide or sodium iodide may be used The initial dose of potassium iodide is 10 drops of a saturated solution diluted in water or milk 3 times daily by mouth This is increased 5 drops with each of the 3 doses daily until the limit of tolerance is reached usually 25–40 drops 3 times daily If sodium iodide is used, 1 Gm in a 10% solution is given daily intravenously and continued for one month after clinical response is obtained

Side effects Lacrimation, metallic taste gastrointestinal upsets, iodide acne and other eruptions

Penicillin and Tetracycline Antibiotics

Indication Actinomycosis

Dose Penicillin—600 000 units intramuscularly daily for 10 days for a total of 6 million units

Tetracyclines—0 5 Gm orally 4 times daily for 25 days

Potassium iodide by mouth may be of value since it destroys granulomatous tissue and so gives the antibiotics access to the organisms within the lesions

an aromatic acrid odor and a bitter taste It is the stuff that knockout drops and Mickey Finns are made of

Indication Chloral hydrate has little or no analgesic activity But as a central nervous system depressant it is used to produce sedation and hypnosis It has a low incidence of skin reactions and is desirable when there is sensitivity to barbiturates

Mechanism of action Chloral hydrate depresses the central nervous system so that ordinary doses cause sedation usually without preliminary excitement in 10–15 minutes and sleep within an hour Sleep lasts for 5 hours and is usually not followed by after-effects although occasionally headache occurs Chloral hydrate is oxidized to trichloroacetic acid in the liver and kidneys and is reduced to trichloroethanol by most tissues The trichloroethanol formed combines with glucuronic acid and the complex is excreted in the urine

Contraindications and side effects This drug is contraindicated in patients with marked hepatic or renal disease Cutaneous side effects include erythema urticaria hemorrhagic and eczematous lesions and exfoliative dermatitis

Dose Adults

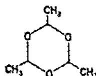
Sedation	0 25 Gm 3 times daily
Sleep	0 5–1 0 Gm at bedtime

Children—Dose in grams for sleep

Newborn	6 mo	1 yr	2 yr	5 yr	10 yr
0 1	0 2	0 3	0 5	0 7	0 8

Available for oral use in 0 25 and 0 5 Gm capsules and as solution containing 0 5 or 0 65 Gm /tsp available as rectal suppositories containing 0 65 or 1 3 Gm.

Paraldehyde



Paraldehyde

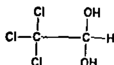
Hypnotics, Sedatives and Tranquilizers

UNTIL 1954 THE ONLY MEANS of allaying anxiety in tense but normal persons and of reducing hyperactivity in the abnormal patient was by administration of sedatives and hypnotics These substances, in the form of barbiturates, chloral hydrate, paraldehyde and bromides, produce their effects of sedation and/or sleep by depressing cortical activity, as well as acting on the reticular formation, of the central nervous system Whether a sedative or hypnotic action predominates is a function of the dose—small doses produce sedation and larger doses, sleep Since then attempts have been made to find agents which will selectively influence subcortical areas of the brain in order to modify different aspects of the individual s reactions to his environment without producing cortical depression and sleep Agents which have the psychopharmacologic effect of making a patient feel calm, relaxed or tranquilized are called tranquilizers or ataractics

HYPNOTICS AND SEDATIVES

For most of the drugs described here, the night time dose for treatment of insomnia is given However, it is possible to use these drugs for daytime sedation by giving approximately one half the evening dose 2 or 3 times during the day

Chloral Hydrate



Chloral hydrate

Chloral hydrate, the first of the artificial hypnotics to be used in medicine, was introduced about 85 years ago It has

Ind ation Phenobarbital is given as a sedative for excitability It must be used with caution becau e skin sensitivity occurs

Mechan sm of action Phenobarbital depresses the central nervous system so that ordinary do es promote calmness within 1 to 2 hours It is not an analgesic Most barbiturates are rather uniformly distributed throughout all tissues Some what higher concentrations are found in the liver and kid neys than in other organs perhaps as a result of a greater degree of protein binding in the e organs The liver plays the most important role in metabolism of the barbiturates Only barbital is eliminated entirely in a chemically un changed form All others are excreted in part in altered form

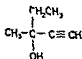
Dose Adults—32 mg orally every 4 to 6 hours

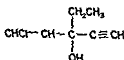
Children	Newborn	6 mo	1 yr	2 yr	5 yr	10 yr
mg	4	6	8	10	12	20

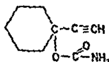
A ailable in tablets containing 16 32 and 65 mg

Side effects and contraindications Skin reactions to pheno barbital include generalized morbilliform rash bullous ery thema multiforme discrete coin sized violaceous macules of fixed drug' type urticaria and exfoliative dermatitis Phenobarbital is tolerated poorly by patients with Addison s disease diabetes mellitus or hyperthyroidism It is contra indicated in the presence of poor hepatic or renal function Addiction may occur

Tertiary Carbinols


Dormison


Placidyl
(Ethchlorvynol)


Valmid
(Ethinamate)

Indication These compounds are effective sedatives and hypnotics and can be used for the treatment of insomnia

Mechanism of action Dormison is metabolized by the kidney

Paraldehyde is a colorless liquid with a characteristic odor and disagreeable burning taste

Indication Paraldehyde is used as a hypnotic Because of the odor it imparts to exhaled air, paraldehyde usually cannot be used for mild sedation in ambulatory patients

Mechanism of action The effects of paraldehyde on the central nervous system resemble those of alcohol However, the action is much more prompt and powerful Ordinary doses cause sleep without preliminary excitement in 10-15 minutes Sleep persists for 4 to 8 hours About 20% of the drug is excreted unchanged through the lungs, about 80% is metabolized to CO_2 and water, presumably by the liver

Contraindications Paraldehyde should not be given in severe bronchopulmonary and hepatic disease because it is metabolized by the liver and excreted by the lungs

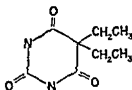
Dose Adults—4–8 ml orally

Children	Newborn	6 mo	1 yr	2 yr	5 yr	10 yr
ml	0 5	0 8	1 0	1 2	2 0	3 0

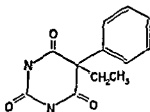
Available as full strength liquid paraldehyde

Barbital and Phenobarbital

The barbiturate group of depressant drugs has been used for sedation, hypnosis or anesthesia Hundreds of derivatives of barbituric acid have been made and tried Of the two included here, barbital was the first to be made and given a trial as a sedative It is mentioned only so that its structure can be shown for comparative purposes Phenobarbital is still one of the most commonly used derivatives of barbituric acid



Barbital



Phenobarbital

TRANQUILIZERS

The development of these drugs until recently has been very slow While agents were being evaluated for antihypertensive activity it was found that rauwolfia products had the additional effect of tranquilizing normal and abnormal persons The anti hypertensive and tranquilizing effects were thought to be due to action on subcortical areas of the brain During this period lysergic acid diethylamide an alkaloid of ergot which contains an indole nucleus as do the rauwolfia alkaloids was found to produce hallucinations and other mental aberrations In 1951 Thorazine structurally related to the antihistamine Phenergan was found to be useful in presurgical anesthesia Later it was shown to affect human behavior Then Miltown related chemically to Tolserol which had been used for several years to treat muscle spasm was found to have sedative properties of an unusual type All these events culminated in the development of a new and very active field—the search for compounds which influence different aspects of individual behavior In dermatology these drugs are important for 2 reasons (1) they are useful in controlling abnormal emotional states accompanying many dermatoses (2) they are responsible for cutaneous drug eruptions

Chemically it is possible to divide the tranquilizers into five groups of compounds phenothiazine rauwolfia alkaloid substituted propanediol diphenylmethane and metathiazanone

Indication Tranquilizers are used as an aid in the treatment of dermatoses that frequently are associated with increased nervous tension These include atopic dermatitis nummular eczema lichen simplex pruritus ani neurotic excoriations psoriasis etc.

Mechanism of action Tranquilizers affect both the central and peripheral components of the nervous system but their dominant role is played in the subcortical areas of the brain They control behavior through their effects on the reticular formation diencephalon and limbic formation The rauwolfia alkaloids and chlorpromazine act in all three of these regions especially in the reticular formation The result of their administration is sedation decreased sensitivity to external stimuli

liver and brain to CO_2 and water The fate of the other two compounds is not known

Dose Adults

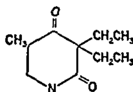
Placidyl—0 5 Gm at bedtime (available in 100, 200, 500 mg capsules)

Valmid—0 5 or 1 0 Gm at bedtime (available in 0 5 Gm tablets)

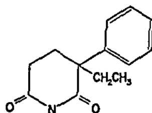
Dormison—0 5 Gm at bedtime (available in 250 and 500 mg capsules)

Side effects Dormison may cause acute exfoliative dermatitis

Piperidinediones



Noludar
(Methyprylon)



Doriden
(Glutethimide)

Indication These compounds are used for the same purpose as the tertiary carbinols, i e , for sedation and sleep

Mechanism of action The depressant action of Noludar on the central nervous system resembles that of the intermediate to short acting barbiturates Sleep ensues within 10–30 minutes and continues for 6 hours The depressant action of Doriden is less than that of phenobarbital Usually a hypnotic dose induces sleep within 30–60 minutes which continues for about 6 hours

Dose Adults

Noludar—200–400 mg at bedtime (available in 50 and 200 mg tablets)

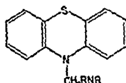
Doriden—0 5 Gm at bedtime (available in 0 25 and 0 5 Gm tablets)

turbing situations in human beings A more basic mechanism of action is not known

No experimental data are available on the mechanism of action of the metathiazanone compound Trancopal

Phenothiazine Derivatives

These drugs have the following basic structure



Thorazine
Vesprin
Compazine
Sparine
Temaril
Trilafon
Dartal
Pacatal
} Tranquilizers

Phenergan
Theruhistin
Pyrrolazote
} Antihistamines

All these drugs are potential photosensitizers Along with the chemical structures of the tranquilizers formulas for some antihistamines are given to show their similarity In addition the phenothiazine and diphenylmethane tranquilizers and the anti histamines have the following core in common —CH_2CH N— In some cases this core is changed slightly but usually it is left intact. For this reason all these drugs tend to overlap in the physiologic properties of being tranquilizers antihistamines antiemetics and anti motion sickness agents The Theruhistin nucleus is similar to but not identical with the phenothiazine nucleus For simplicity the salts of these substances that are available commercially are not illustrated The molecular weight of the salt—whether it is a hydrochloride tartrate etc —determines in part the over all tablet size and dose

and depression of sympathetic activity and skeletal muscle tone

Reserpine activates release of the neurohormone serotonin in the brain and, in a direct peripheral action, depletes the peripheral nerve endings of nor epinephrine The onset of action of reserpine is slower than that of chlorpromazine, the peak effect occurring several hours after administration Reserpine is in the body for only a few hours, but the impairment of serotonin storage mechanisms persists for a long time

Chlorpromazine does not affect serotonin It may interfere with the action of nor epinephrine Chlorpromazine can block the peripheral action of epinephrine, but this is not its chief function In addition it has antihistamine activity and is a potent local anesthetic Unlike reserpine the effects of chlor promazine are prompt and reach a peak within one hour Nearly all chlorpromazine taken by mouth is metabolized Little is excreted in the urine as such About 15% of chlorpromazine given intravenously is excreted in the urine as the sulfoxide The latter has many of the pharmacologic properties of the free compound but is much less active

Less is known of the mechanism of action of the substituted propanediols and diphenylmethane drugs The former, of which Miltown and Equanil are well known examples, cause changes in spontaneous electrical activity of the cortex and thalamus and depress polysynaptic reflexes in the spinal cord In the usual clinical doses there are no effects outside the central nervous system Their action begins soon after administration and lasts for a few hours Ten per cent of meprobamate is excreted unchanged in the urine Another fraction is conjugated before excretion and the remainder is metabolized to unknown products Tolseram but not Tolserol can reduce the pituitary output of MSH (melanocyte stimulating hormone) to normal in patients with alopecia areata Such patients ordinarily excrete excessive amounts of MSH in the urine

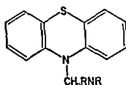
The diphenylmethane compounds have some antiacetyl choline like activity on tissues outside the central nervous system They reduce autonomic responses to emotionally dis

turbing situations in human beings A more basic mechanism of action is not known

No experimental data are available on the mechanism of action of the metathiazanone compound Trancopal

Phenothiazine Derivatives

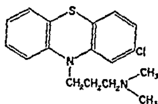
These drugs *have the following basic* structure



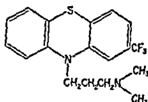
Thorazine Vesprin Compazine Sparine Temaril Trilafon Dartal Pacatal	Tranquilizers
Phenergan Theruhistin Pyrrolazote	Antihistamines

All these drugs are potential photosensitizers Along with the chemical structures of the tranquilizers formulas for some antihistamines are given to show their similarity In addition the phenothiazine and diphenylmethane tranquilizers and the anti histamines have the following core in common $—CH_2CH\ N—$ In some cases this core is changed slightly but usually it is left intact For this reason all these drugs tend to overlap in the physiologic properties of being tranquilizers antihistamines antiemetics and anti motion sickness agents The Theruhistin nucleus is similar to but not identical with the phenothiazine nucleus For simplicity the salts of these substances that are available commercially are not illustrated The molecular weight of the salt—whether it is a hydrochloride tartrate etc —determines in part the over all tablet size and dose

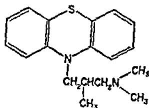
PHENOTHIAZINE



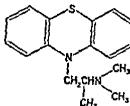
Thorazine
(Chlorpromazine)



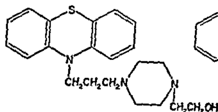
Vesprin
(Triflupromazine)



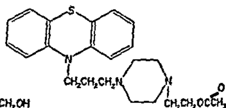
Temaril
(Trimeprazine)



Phenergan
(Promethazine)

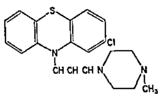


Trilafon
(Perphenazine)

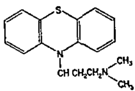


Dartal
(Thiopropazate)

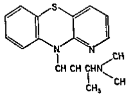
Compounds



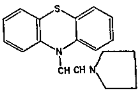
Compazine
(Prochlorperazine)



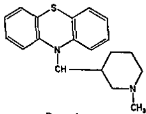
Sparine
(Promazine)



Theruhistin
(Isothipendyl)

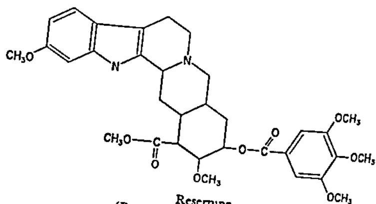


Pyrrolazote
(Pyrathiazine)

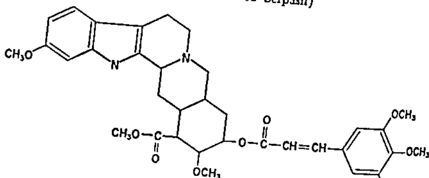


Pacatal
(Mepazine)

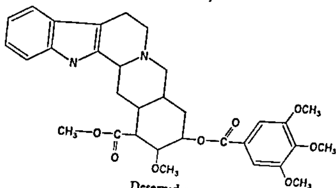
Rauwolfia Alkaloids



Reserpine
(Reserpoid Rau Sed Serpasil)



Rescinnamine
(Moderil)

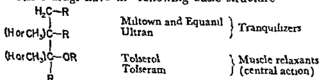


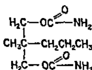
Deserpidine
(Harmonyl)

Alkaloids are organic basic substances found in plants The rauwolfia alkaloids of which Rauwolfia serpentina Benth is the best known species are woody plants which grow in tropical areas The 3 pure rauwolfia alkaloids used in medicine today are reserpine rescinnamine and deserpidine These compounds are used for their hypotensive effects in hyper tension and their tranquilizing effects in emotional disorders The rauwolfia alkaloids and lysergic acid derivatives have an indole nucleus which makes them similar in structure to serotonin and melatonin

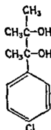
Substituted Propanediol Compounds

These drugs have the following basic structure

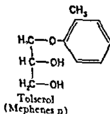




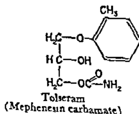
Miltown Equanil
(Meprobamate)



Ultran
(Phenaglycodol)

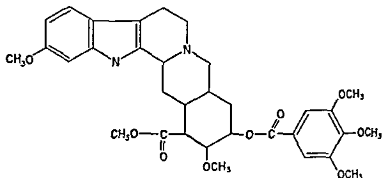


Tolserol
(Mephenesin)

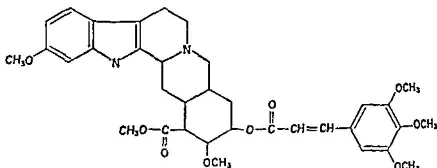


Tolseram
(Mephenesin carbamate)

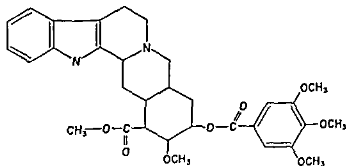
Rauwolfia Alkaloids



Reserpine
(Reserpoid Rau Sed Serpasil)



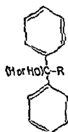
Rescinnamine
(Moderil)



Deserpidine
(Harmonyl)

Diphenylmethane Compounds

These drugs have the following basic structure

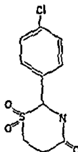


Drugs	Use
Suavitil Frenquel Atarax Vistaril	Tranquilizers
Benadryl Ambodryl Dimetane* Diafen Perazil	Some representative antihistamines
Dramamine Bonamine	For prevention and treatment of motion sickness

For comparison the structural formulas of 10 diphenylmethane drugs are given It will be noted that 3 are tranquilizers 5 are antihistamines and 2 are used for the prevention and treatment of motion sickness

Metathiazanone

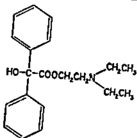
The only compound of this type available at present is Trancopal (Winthrop)



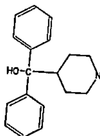
Trancopal

*The chemical nucleus of Dimetane is similar to but not identical with the diphenylmethane nucleus.

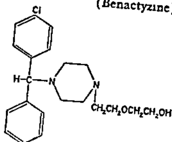
DIPHENYLMETHANE COMPOUNDS



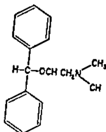
Suavitil
(Benactyzine)



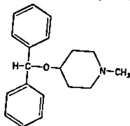
Frenquel
(Azacyclonol)



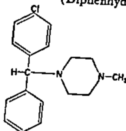
Atarax Vistaril
(Hydroxyzine)



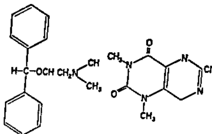
Benadryl
(Diphenhydramine)



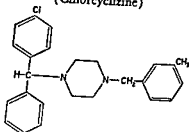
Diafen
(Diphenylpyraline)



Perazil
(Chlorcyclizine)



Dramamine
(Dimenhydrinate)



Bonamine
(Meclizine)

compound of this type Tolseram but not Tolserol can cause light bands of decreased pigmentation of the scalp hair in brown haired persons

Diphenylmethane compounds Erythematous papular eruptions may occur from direct contact with the drug or following systemic administration Drowsiness and dizziness occur

Metathiazanone Dermatitis flushing dizziness nausea and weakness may occur

Dose of Tranquilizers

These compounds are prepared in different strengths and in various forms such as tablets capsules solutions suppositories and sustained release preparations The usual oral doses of some common tablet forms are given below

	Adults 3-4 Times Daily	Children 3-4 Times Daily
Phenothiazine compounds		
Thorazine 10 25 50 100 mg	25 mg	0 25 mg /lb body wt
Vesprin 10 mg	10 mg	
Compazine 5 10 mg	5 mg	5 mg
Sparine 10 25 50 100 200 mg	10–25 mg	
Temaril 2 5 mg	2 5 mg	
Trilafon 2 4 8 16 mg	2–4 mg	
Dartal 5 10 mg	5 mg	
Pacatal 25 50 100 mg	25 mg	
Phenergan 12 5 25 mg	12 5–25 mg	
Rauwolfia alkaloids		
Reserpine		
Reserpoid 0 1 0 25 1 0 4 mg	0 1 mg	
Rau Sed 0 1 0 25 0 5 1 0 mg	0 1 mg	
Harmonyl 0 1 0 25 1 mg	0 1 mg q d	
Moderil 0 25 0 5 mg	0 25 mg q d	

Chiefly for psychoses

Side Effects and Toxic Reactions of Tranquilizers

Phenothiazine compounds These compounds are photosensitizers, and often a pronounced long lasting erythema is observed They should not be given to any patient receiving ultraviolet light therapeutically, as in psoriasis or atopic dermatitis because of the possibility of inducing photosensitizing reactions. Dermatitis may occur with or without exposure to ultraviolet light Erythema and papules may result from direct contact with the drug and through oral or parenteral administration Purpura, urticaria and erythema multiforme like eruptions may occur Systemic side reactions include an exaggeration of therapeutic effects, such as drowsiness and lethargy Jaundice, parkinsonian like neurologic findings, orthostatic hypotension and blood dyscrasias may occur These drugs should be withheld in liver disease

If a patient is sensitive to a particular phenothiazine compound, e g , Thorazine or Phenergan, but requires further therapy, it is advisable to check structural formulas in order to select a drug to which cross sensitization might not be expected to occur

Rauwolfia alkaloids Purpura and ecchymoses may occur Exaggerated therapeutic effects such as lethargy, fatigue and muscle weakness may develop Other systemic effects include confusion, paranoia, depression leading to suicide, nightmares and anxiety bradycardia and hypotension increased motor and secretory activity of the gastrointestinal tract leading to increased food intake and weight gain gastritis diarrhea hemorrhage nasal stuffiness and epistaxis Rauwolfia alkaloids should not be given to depressed patients

Substituted propanediols Cutaneous reactions to meprobamate therapy include purpuric, eczematous erythematous and papular skin eruptions Systemic reactions include weakness severe sedation with inability to stand or walk, nausea and vomiting Sudden withdrawal of the drug may be followed by anorexia, vomiting anxiety insomnia, tremors, muscle twitching, hallucinations or grand mal seizures A ' let down" feeling often occurs soon after initiating therapy with any

compound of this type Tolseram but not Tolserol can cause light bands of decreased pigmentation of the scalp hair in brown haired persons.

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Sparine 10 25 50 100 200 mg	10–25 mg	
Temaril 2.5 mg	2.5 mg	
Trilafon 2 4, 8 16 mg	2–4 mg	
Dartal 5 10 mg	5 mg	
Pacatal 25 50 100 mg	25 mg	
Phenergan 12.5 25 mg	12.5–25 mg	
Rauwolfia alkaloids		
Reserpine		
Reserpoid 0 1 0.25 1.0 4 mg	0 1 mg	
Rau Sed 0 1 0 25 0.5 1.0 mg	0 1 mg	
Harmonyl 0 1 0 25 1 mg	0 1 mg q.d.	
Moderil 0 25 0.5 mg	0.25 mg q d	

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Phenergan 12 5 25 mg	12.5–25 mg	
Rauwolfia alkaloids		
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Harmonyl 0 1 0 25 1 mg	0 1 mg q d	
Moderil 0 25 0.5 mg	0 25 mg q d	

Chiefly for psychoses

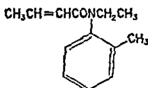
	Adults 3-4 Times Daily	Children 3-4 Times Daily
Diphenylmethane derivatives		
Suavitil		
1 mg	1 mg	
Frenquel		
20, 100 mg	100 mg t.i d initially, 20 mg q d maintenance	
Atarax		
10 25, 100 mg	25 mg	3–6 yr 10 mg 6 yr 20 mg
Benadryl		
25 50 mg capsules	50 mg	10–20 mg
Substituted propanediols		
Miltown and Equanil		
200 400 mg	400 mg	3 yr 100 mg
Ultran		
300 mg capsules	300 mg	
Tolserol		
0 25 0 5 Gm	1 Gm	
Tolseram		
0 5 Gm	1 Gm	
Metathiazanone		
Trancopal		
100 mg	100 mg	

Insecticides and Insect Repellents

Insecticides and insect repellents differ from one another Whereas an insecticide is lethal to an insect it may be incapable of repelling the insect or preventing its bite On the other hand, an agent may be a repellent without having insecticidal activity Some agents exert both actions

Eurax (Geigy)

Eurax contains 10% N ethyl o crotonotoluide



N Ethyl-o crotonotoluide

Indication For the prevention and treatment of scabies Also may be used as a nonspecific antipruritic its mode of action in this regard being unknown

Mode of action Scabicidal

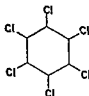
Application Before bedtime the cream or lotion should be massaged into the skin of the entire body from the chin down paying particular attention to the interdigital spaces flexor surfaces of the wrists inner and outer aspects of the elbows axillae undersurface of the breasts the umbilicus buttocks and inner aspects of the thighs This procedure should be repeated the following night Preliminary bathing or scrubbing is not necessary A cleansing bath may be taken 24 hours after the second application A complete change of clothing and bed linen should be made the morning after the last application and the previously used garments and linen should be laundered or dry cleaned To avoid relapse all members of an infected household should be thoroughly examined and all contacts should receive prophylactic treatment

Contraindication Do not apply Eurax to acutely inflamed skin or to raw weeping areas

Available as a 10% cream in 20 and 60 Gm tubes and as a 10% lotion in 2 and 6 oz bottles

Kwell (Reed & Carnrick)

Kwell contains 1% lindane the gamma isomer of 1 2 3 4 5 6 hexachlorocyclohexane



Lindane
(1 2 3 4,5 6 hexachlorocyclohexane)

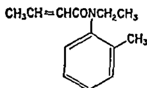
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Diphenylmethane derivatives		
Suavitil		
1 mg	1 mg	
Frenquel		
20, 100 mg	100 mg t i d initially 20 mg q d maintenance	
Atarax		
10 25, 100 mg	25 mg	3–6 yr 10 mg 6 yr 20 mg
Benadryl		
25, 50 mg capsules	50 mg	10–20 mg
Substituted propanediols		
Miltown and Equanil		
200 400 mg	400 mg	3 yr 100 mg
Ultran		
300 mg capsules	300 mg	
Tolserol		
0 25 0 5 Gm	1 Gm	
Tolseram		
0 5 Gm	1 Gm	
Metathia anone		
Trancopal		
100 mg	100 mg	

Insecticides and Insect Repellents

INSECTICIDES AND INSECT REPELLENTS differ from one another Whereas an insecticide is lethal to an insect, it may be incapable of repelling the insect or preventing its bite On the other hand, an agent may be a repellent without having insecticidal activity Some agents exert both actions

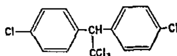
Eurax (Geigy)

Eurax contains 10% N-ethyl o crotonotoluide



N Ethyl-o-crotonotoluide

DDT



DDT
(Dichlorodiphenyl trichloroethane)

Indication For prevention and treatment of pediculosis

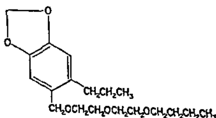
Mode of action DDT kills mature lice and larvae but not nits However it remains on the skin and clothing long enough for ova to develop and be destroyed at that time If DDT does not kill all the lice add 0 2% pyrethrins or use lindane and pyrethrin powder

Application Dust into clothing and onto skin

Available as 2% DDT emulsion or 10% DDT in talcum powder

Emulsifiable Pyrenone 10 1 (Fairfield Chemicals)

This repellent contains 10% piperonyl butoxide and 1% pyrethrin Piperonyl butoxide is a technical product containing 80% pure (3 4 methylene dioxy 6 propyl benzyl) (butyl) diethylene glycol ether



Piperonyl butoxide

Indication For prevention and treatment of scabies, pediculosis and chigger infestations and to repel ticks and other arthropods

Mode of action Scabicidal and pediculicidal

Application See Eurax

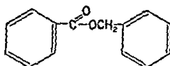
Available as a cream in 60 Gm jars and as a lotion in 2 oz bottles

Topocide (Lilly)

Topocide is an aqueous emulsion of benzyl benzoate

Benzyl benzoate	12 5%
Benzocaine	2 %
DDT	1 %

Water, bentonite magma and polyoxyalkylene sorbitan mono-oleate comprise the inert ingredients



Benzyl benzoate

Indication For treatment of pediculosis (Pediculus capitis and Phthirius pubis) and scabies

Mode of action Scabicidal and pediculicidal

Application (1) Scabies Following a soapy bath, rub Topocide into dry skin with gauze sponges Allow to dry After each washing apply lotion to hands only Do not bathe for at least 24 hours Treat clothing as described under Eurax

(2) Head lice Wash hair with regular shampoo When hair is dry, anoint scalp and comb hair to spread medication Leave on for 10 days Repeat in 2 or 3 weeks if necessary

(3) Pubic lice Apply to affected parts, leave Topocide on for 2 days and then wash off

Caution Protect eyes from medication Do not reapply except to hands for 10–15 days

Available in 4 oz bottles

Indication mode of action application See Emulsifiable Pyrenone 10–1

Available as Triple mix Repellent Liquid in 2 oz bottles or Creme in 1 or 2 oz tubes the latter containing 94% of the liquid with 6% carnauba wax.

Skat (J W Williams)

Rutgers 612 (2 ethyl 1 3 hexanediol)	70%
Alcohol	30%

Indication mode of action application See Emulsifiable Pyrenone 10–1

Available in 50 Gm. bottles

6-12 Insect Repellent (Union Carbide)

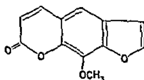
This compound is 100% Rutgers 612 (2-ethyl 1 3 hexanediol)

Indication mode of action application See Emulsifiable Pyrenone 10–1

Light Protective Agents

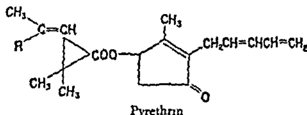
ORAL

Methoxsalen (Oxsoralen Elder Meloxine Upjohn)



8 Methoxypsoralen
(8 MOP methoxsalen Oxsoralen Meloxine)

8 Methoxypsoralen has the unusual property of increasing the biologic effects of light in the region of 3 600 Å When



Pyrethrin

In pyrethrin I, R is CH_3

In pyrethrin II, R is $COOCH_3$

Indication For use as a repellent against mosquitoes, flies, chiggers, ticks, fleas, etc Confers protection for 2 to 6 hours after application

Mode of action Insecticidal

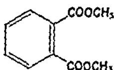
Application For use as a tactile repellent apply to skin before exposure to insects Repeat every 2 to 6 hours depending upon degree of perspiration The chemical may be applied to clothing in a spray after it is diluted 1 9 with water

Available in 2 oz bottles

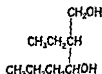
Insect Repellent 622 (Fairfield Chemicals)

This preparation, also known as Triple mix Repellent Liquid, contains the following substances

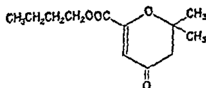
6 parts dimethylphthalate
2 parts indalone
2 parts Rutgers 612



Dimethylphthalate



Rutgers 612
(2 Ethyl 1,3 hexanediol)



Indalone
(Butopyronoxyl)

intensity comes out of the solution in the line of the incident beam and light of a longer wavelength (fluorescence) is produced in the solution and comes out at all angles to the incident beam These two optical properties absorption and fluorescence are measured easily Psoralen 8 methoxypsoralen and trimethylpsoralen have almost identical ultraviolet light absorption curves Maximum absorption is at about 2 490 Å However the optimum wavelength to produce fluorescence for all three compounds is 3 600 Å The fluorescent light emerging from the solutions is most intense from 4 200 to 4 600 Å The optimum wavelength for biologic activity appears to be related not to the light absorption maximum or fluores cence maximum but to the optimum wavelength—3 600 Å—to produce fluorescence At 3 600 Å psoralen is 2 3 times more activated than 8 methoxypsoralen and trimethylpsoralen is 15 times more activated

Dose 10–20 mg orally 1 to 3 hours before exposure to ultra violet light It is important to keep the exposure time within prescribed limits during the first 3 to 4 days in order to acquire skin changes that will afford protection against subsequent exposure If the patient takes 20 mg of 8 methoxypsoralen and on the first day exposes himself to intense sunlight for one or more hours rather than for the recommended time he will develop marked erythema edema and blistering of the skin A sun exposure guide suggested by Fitzpatrick is as follows

EXPOSURE IN MINUTES

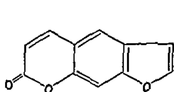
Basic Skin Color	Initial	2d	3d	4th	Subsequent Exposures
Light	15	20	25	30	Gradually increase based on erythema and tenderness
Medium	20	25	30	35	

Side effects Side effects are uncommon Most frequently encountered are nausea increased nervous tension and insomnia The view that 8-methoxypsoralen causes liver damage has not been substantiated

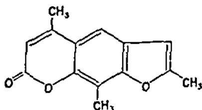
Contraindications 8 Methoxypsoralen should not be given to patients who have illnesses associated with light hyper

approximately 20 mg of this substance is taken orally, increased tanning and decreased burning occur following exposure of the skin to sunlight. When 50 mg or more is taken all the reactions of skin to light are increased These include pigmentation, erythema, thickening of the keratin layer, etc Within a few days after ingesting 8 methoxypsoralen and exposing the skin to sunlight, the tanning and keratin formation responses become pronounced, with a subsequent decrease in the erythematous reaction In this way 8 methoxypsoralen can prevent burning of skin from ultraviolet light and increase the tanning response The drug has no effect when given without subsequent exposure of the skin to light When 8 methoxypsoralen is added to cultures of some bacteria and fungi and the latter are exposed to ultraviolet light inhibition of growth occurs

Psoralen derivatives occur naturally in a variety of plants throughout the world, and new ones can be made synthetically These natural and synthetic psoralens vary in their capacity to augment tanning and erythema When applied topically the basic nucleus, psoralen, is the most potent producer of erythema following exposure of skin to sunlight Trimethyl psoralen is the second most potent psoralen Both of these substances are more active than 8 methoxypsoralen However, only 8 methoxypsoralen has been thoroughly studied in vivo in man The trimethylpsoralen looks promising because it is not only more potent than 8 methoxypsoralen when applied topically but is also without apparent toxicity in animals

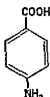


Psoralen



4 5 8 Trimethylpsoralen (TM)

When light of a given wavelength passes through a solution containing a psoralen compound, two things happen Light of the same wavelength and of either the same or of reduced



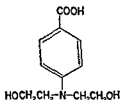
Para aminobenzoic acid

TiO
Titanium dioxide

Mode of action PABA absorbs ultraviolet light in the region of 2 500–3 100 Å Titanium dioxide is an opaque substance which absorbs throughout the entire light spectrum
Available on prescription

Skolex (Williams)

P dihydroxyethyl aminobenzoic acid 5%
In water washable base



P-dihydroxyethyl aminobenzoic acid

Mode of action See PABA
Available in 2 oz. bottles

Skol (Williams)

P-dihydroxyethyl aminobenzoic acid 5%
In a lotion
Available in 8 oz bottles

sensitivity, such as lupus erythematosus or polymorphous light eruptions

Carotene

Indication Oral administration of carotene may be useful in patients in whom exposure to light of the visible spectrum results in urticaria

Mode of action Carotene deposited in the skin after oral administration absorbs visible light to reduce the action of the light on the skin

Dose 50,000 units (based on vitamin A activity) daily

Available in capsules containing 25 000 units of vitamin A activity

Chloroquine and Plaquenil

These drugs are discussed in the next section, Lupus Erythematosus and Light Sensitivity Eruptions Since these drugs are so helpful in patients with polymorphous light eruptions, they should be tried in patients who have other types of light sensitivity diseases

TOPICAL

Topical preparations to protect against sunlight contain agents that either are opaque to light—such as titanium dioxide—or compounds that absorb light in certain regions of the spectrum—such as para and ortho aminobenzoic acid derivatives, tannic acid derivatives, etc Light protective ointments are applied to areas likely to be exposed to sunlight They are effective for periods up to 4 hours, depending on the amount of perspiration These preparations are used in disorders aggravated by ultraviolet radiation e g, lupus erythematosus, and when melanin pigmentation is undesirable, as in melasma of pregnancy

PABA Ointment

Para aminobenzoic acid	10%
Titanium dioxide	5%
In water washable base	

A Fil Sun Stick (Texas Pharmacal)

Digalloyl trioleate 2.5¢
In a wax stick

This stick can be applied to the lips for protection against ultraviolet light.

Lupus Erythematosus and Light Sensitivity Eruptions

ANTIMALARIALS

ARALEN PLAQUENIL ATABRINE AND CAMOQUIN are useful in the therapy of lupus erythematosus (systemic and discoid) and for the prevention of some light sensitivity eruptions

When the lesions of lupus erythematosus are confined primarily to the skin the patient can be treated with the antimalarial drugs alone When the disease is chiefly systemic steroids alone may be used However for most patients with systemic involvement it is best to use a combination of steroids and antimalarials in order to keep the dose of steroids as low as possible and to obtain a greater therapeutic effect.

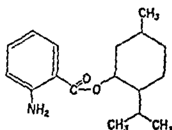
When a single antimalarial is used the drug of choice is either Aralen or Plaquenil At times the patient will respond to one better than to the other Atabrine is not used alone because to obtain a satisfactory therapeutic effect sufficient Atabrine must be given to make the skin yellow Also Atabrine is perhaps the most toxic of the 4 drugs Agranulocytosis has resulted from Atabrine and Camoquin but not from Aralen and Plaquenil One preparation is available (Triquin) which contains 3 of the antimalarials

Mechanism of action The antimalarials have some properties similar to those of riboflavin In rats Atabrine increases the excretion of riboflavin and promotes the growth of young animals given suboptimal amounts of riboflavin Aralen Plaquenil and Atabrine have structures that are similar not only to riboflavin but also to Apresoline Apresoline can

A Fil (Texas Pharmacal)

Menthyl anthranilate	5%
Titanium dioxide	5%

In a water washable base



Menthyl anthranilate

The active part of menthyl anthranilate is the ortho-aminobenzoic acid nucleus The light absorption of this compound is similar to that of para aminobenzoic acid
Available in 2 oz tubes

Neo A Fil (Texas Pharmacal)

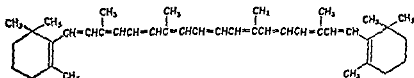
Digalloyl trioleate	3%

In a water washable base

Digalloyl trioleate consists of a mixture of 3 derivatives of tannic acid and absorbs ultraviolet light in the region of 2,900 through 3,150 Å
Available in 2 oz tubes

Carotene Ointment

Carotene absorbs light in the region of 4,000–5,000 Å An ointment containing this compound can be made by adding 50 000 units of beta carotene to each gram of water washable base



Beta-carotene

A Fil Sun Stick (Texas Pharmacal)

D galloyl trioleate 25%
In a wax stick

This stick can be applied to the lips for protection against ultraviolet light.

Lupus Erythematosus and Light Sensitivity Eruptions

ANTIMALARIALS

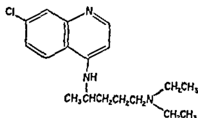
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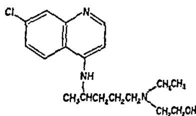
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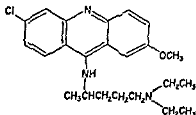
produce lupus erythematosus in man, whereas the antimalarials are used to treat this disease Thus *one gets the impression that* lupus erythematosus is a metabolic disorder involving the metabolism of the flavinoids related to riboflavin and that *the antimalarials can correct this biochemical defect*



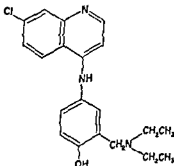
Aralen
(Chloroquine)



Plaquenil
(Hydroxychloroquine)



Atabrine
(Quinacrine)



Camoquin
(Amodiaquin)

Dose

Aralen phosphate (Winthrop)—250 mg 2–3 times daily for 2–4 weeks After a good response, the dose is reduced gradually to 250 mg daily
Available in 250 mg tablets

Plaquenil sulfate (Winthrop)—The required dose of Plaquenil usually is greater than that of Aralen The initial dose may be 200 mg 6 times daily with gradual reduction to 200 or 400 mg daily
Available in 200 mg tablets

Atabrine hydrochloride (Winthrop)—100 mg 3 times daily until improvement or until the skin becomes yellow, followed by 100 mg as the daily maintenance dose The white count should be checked weekly

Available in 100 mg tablets

Triquin (Winthrop)—This drug is a mixture of Aralen phosphate 65 mg Plaquenil sulfate 50 mg and Atabrine hydrochloride 25 mg One tablet 3 to 4 times daily until a good response is obtained after which the dose may be reduced slowly to 1 tablet daily

Camoquin (Parke Davis)—200 mg 3 times daily after meals for 2 weeks The dose is then reduced to 200 mg 2 times daily The white count should be checked weekly

Available in 200 mg tablets

Side effects

Chloroquine frequently causes the formation of opacities in the corneal epithelium resulting in blurred vision and halos around light These changes have been reversed by either decreasing the dose or discontinuing the drug Urticaria and exfoliative dermatitis have occurred Spectacular changes in hair color may take place Blond red and brown hair may grow out in a light blond shade This effect is reversible Leukopenia may occur

Caution Chloroquine should not be given to patients with psoriasis because it may aggravate this disease

Plaquenil is almost identical in chemical structure to chloroquine so that similar side effects may occur

Atabrine has been associated with skin eruptions and agranulocytosis

Camoquin sometimes causes vertigo One patient developed jaundice lethargy anorexia and partial blindness These symptoms cleared on cessation of the drug Agranulocytosis has occurred

All the antimalarials can produce gastrointestinal reactions such as nausea and vomiting

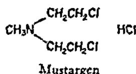
STEROIDS

Oral steroid preparations are given to patients with acute lupus erythematosus (see section on Steroids and ACTH) After the disease is satisfactorily controlled, the steroid dose is reduced slowly to the minimum required to maintain the patient free from symptoms At this stage the antimalarials may be added and an additional attempt made to lower the steroid dose even further

Topically, 1% hydrocortisone or 0 5% prednisolone preparations have little or no effect on the cutaneous lesions of lupus erythematosus However, 0 25% fluorohydrocortisone, 2 5% hydrocortisone and 0 1–0 5% triamcinolone acetonide are effective and should be used in conjunction with chloroquine derivatives

Nitrogen Mustard Therapy

Mustargen (Merck, Sharp & Dohme)



Mustargen

(2 2 Dichloro-N methyldiethylamine hydrochloride methyl bis (β chloroethyl) amine hydrochloride HN_2 hydrochloride)

Indication Mycosis fungoides tumor stage Has been used in some selected cases of systemic lupus erythematosus

Mode of action Depresses lymphoid tissue

Dose 0 1 mg/kg of body weight each day, or every other day for 4 doses the total amount for a single injection not to exceed 8 mg The solution should be freshly prepared each time, and the calculated volume should be injected into

the tubing of a running intravenous infusion 50 mg of Benadryl may be given intravenously at the same time to help allay nausea

Mustargen has been used in treatment of some cases of systemic lupus erythematosus which have not responded to other forms of therapy Great caution must be exercised in giving nitrogen mustard to these patients because they often have severe leukopenia to begin with

Available in sets of four 20 ml vials each containing 10 mg of drug in dry form triturated with 90 mg of anhydrous sodium chloride

Side effects Nausea vomiting agranulocytosis The white blood cell count should be followed closely because of the possibility of agranulocytosis developing This may appear approximately one week after the course of treatment It may be advisable to protect the patient with combinations of antibiotics until the period of agranulocytosis is past, usually about 3 weeks after the end of therapy

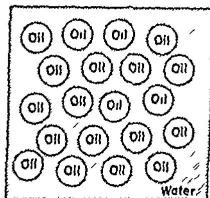
Caution Mustargen should not be allowed to come in contact *with skin or mucous membranes for vesication may occur* It should not be given to pregnant women because although results of treatment during pregnancy in human beings are not known malformations of the fetus have occurred in rats

Ointment Bases and Lubricating Agents

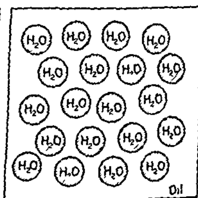
BECAUSE OF THEIR physical properties ointments are used in dermatologic therapy for 3 purposes (1) as lubricating agents (2) as vehicles in which to incorporate drugs required to treat skin disorders and (3) as protective coverings not only to prevent contact of the skin surface with noxious agents but to reduce heat loss

Ointments are commonly classified into 3 types oil in water

(O/W), water in oil (W/O) and inert oil The last named includes petrolatum, mineral oil and Carbowax The O/W and W/O ointments are emulsions The relative amounts of water and oil and the nature of the emulsifying agent determine the type of emulsion The term *oil in water* indicates that oil droplets, the discontinuous phase, are dispersed in water, the continuous phase The term *water in oil* indicates that droplets of water, the discontinuous phase, are dispersed in oil, the continuous phase



Oil in water (o/w)



Water in oil (w/o)

The general term *oil* includes oils, fats and waxes In addition to water and oil these emulsions also contain wetting and emulsifying agents, such as Tweens Spans Tritons spermaceti and gum tragacanth and preservatives to prevent mold growth Common preservatives are methylparaben and propylparaben, the methyl and propyl esters of hydroxybenzoic acid The emulsions may contain a suspending agent, such as methyl cellulose and perfumes

The terms *salve, ointment* and *cream* indicate preparations that have in common the properties of being semisolids which are spread easily on skin While these terms can be used interchangeably they are sometimes thought to represent gradations in viscosity, the salve being considered most viscous the ointment less and the cream least

Indication The O/W emulsions are indicated when vehicles which are penetrating water washable and not greasy to the

touch are desired They may be preferred for cosmetic reasons For lesions on the scalp they are most suitable because they can be easily washed out of the hair For protection against ultraviolet light O/W vehicles seem to be the most effective The W/O emulsions are used to provide lubrication and are especially indicated when the skin is dry O/W or W/O preparations are required for penetration of drugs Penetration with all bases is greatly increased if nonionic surface active agents such as Tween or Span are present Consequently drugs incorporated into bases containing these agents must be used in smaller concentration than otherwise The inert oil bases are used when an occlusive layer on the skin surface is needed Some of the inert oil bases can be defatting because they supply no natural oils to the skin but instead extract some They do not facilitate penetration of drugs For psoriatic lesions on glabrous skin petrolatum seems to be a more effective base than O/W or W/O compounds To prevent heat loss as occurs in an extensive chronic, exfoliative dermatitis petrolatum or the W/O bases are best For most antibiotics inert oil or W/O bases offer greater stability than O/W emulsions Carbowax differs from the other inert oils such as petrolatum and mineral oil in being miscible with water either from the skin or from other sources By mixing inert oils with O/W or W/O emulsions bases with combinations of properties—such as lubrication penetration and protection—can be achieved

At present it is not possible to list completely the specific ointment in which to put a particular drug for the best treatment of a given disorder There have been few systematic attempts to evaluate the influence of the ointment base on penetrability or therapeutic effectiveness of a drug More studies must be done using paired controls With this method it was found that in the case of psoriasis petrolatum was a better ointment in which to incorporate drugs than other bases By measuring the local skin reaction produced after incorporating an irritating substance such as corrosive sublimate ($HgCl_2$) in a base it was found that a positive reaction occurred with many bases but a negative one with Carbowax Thus in one experiment Carbowax did not allow

release of enough corrosive sublimate to react with the skin

The surface active agents such as Tween and Span increase the penetration of drugs For example, if a sensitizing agent such as paraphenylenediamine is incorporated into 2 bases—one containing Tween and one without Tween—the skin shows more reaction to the base containing Tween In addition it is possible with the aid of these detergents to detect a sensitivity reaction where none was evident before the base containing Tween was applied In all probability Tween facilitates the penetration of the sensitizing agent into the skin

Some Known Indications for Various Ointment Bases

O/W	W/O	Inert Oil
1 Ultraviolet screening agents	1 Lubrication	1 Retain heat
2 Scalp preparations	2 Retain heat	2 Antibiotics
3 Penetration desired	3 Penetration desired	3 Psoriasis
4 Cosmetic elegance	4 Antibiotics	
	5 Psoriasis	

Perhaps in the future attempts will be made to determine the base that allows for greatest absorption of a given drug and the base that makes possible the greatest therapeutic effect of a drug or mixture of drugs Only after these data are obtained can it be decided which base to use to produce a good therapeutic response

Mode of action As a vehicle for incorporated drugs the water in oil types of ointment and inert oils occlude the skin surface This leads to suppression of evaporation and swelling of the cells in the horny layer which may allow for greater penetration of drugs incorporated in the ointment The oil in water or water washable bases enable the added drugs to penetrate by effecting close contact with the skin cells Ointments also carry drugs into the sebaceous glands where they may have a local effect or be absorbed into the systemic circulation As mentioned previously the surface active agents increase penetration

Vanishing creams are oil in water emulsions which disappear without forming clumps upon application to the skin These creams usually contain stearic acid and a relatively high percentage of water

Cold creams are oil in water or water in-oil emulsions

characterized by a preponderance of oil They are the cosmetic creams such as night cream emollient cream cleansing cream and all purpose cream Cold cream itself is commonly made with mineral oil beeswax water and borax The creams usually have an alkaline reaction because a soap is formed from borax and beeswax. Cleansing and liquefying properties may be increased by the use of a smaller percentage of wax and a higher percentage of mineral oil An emollient or night cream contains less wax or mineral oil which is compensated for by an equivalent amount of vegetable oil animal oil or fat

Oil in Water or Water Washable Bases

Almay Emulsion Base (Almay)

This base contains fatty acid and glycol esters spermaceti cetyl alcohol propylene glycol and water

Unibase (Parke Davis)

Unibase contains higher fatty alcohols petrolatum glycerin water and an emulsifying agent.

Neobase (Burroughs Wellcome)

Neobase contains polyhydric alcohol esters propylene glycol water and a small amount of liquid petrolatum As a preservative against molds 0 3% methyl p-hydroxybenzoate is present The pH is approximately 3 4

Dermabase (Marcelle)

Dermabase contains stearyl alcohol glyceryl monostearate spermaceti propylene glycol mineral oil water a preservative and an emulsifying agent

Cetaphil (Texas Pharmacal)

Cetaphil contains cetyl alcohol stearyl alcohol propylene glycol sodium lauryl sulfate and water

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Cold creams are oil in water or water in-oil emulsions

and more occlusive effect anhydrous lanolin should be specified

Hydrosorb (Abbott)

Hydrosorb is a mixture of the oleic acid ester and amide of diethanolamine oleic acid and white petrolatum

Polysorb (E Fougera)

Polysorb contains sorbitan sesquioleate in a wax petrolatum mixture

Velvachol (Texas Pharmacal)

Velvachol contains cholesterol sodium lauryl sulfate cetyl alcohol stearyl alcohol petrolatum mineral oil and water

Qualatum (Almay)

Qualatum contains 93% of a mixture of petrolatum and mineral oil and 7% polyhydric fatty acid esters

Inert Oil

Yellow Petrolatum

Petrolatum or petroleum jelly is a purified mixture of semisolid hydrocarbons obtained from petroleum

White Petrolatum

White petrolatum or white petroleum jelly is petrolatum wholly or nearly decolorized Usually no chemicals are used for decolorization Yellow petrolatum is repeatedly passed through a filter bed of bauxite or fullers earth at 120–200 F to remove coloring matter

Carbowax Ointment (Union Carbide & Carbon)

Carbowax 1,500	55%
Carbowax 4 000	20%
Polyethylene glycol 300	25%

The Carbowaxes and polyethylene glycols which are soluble in water are mixtures of polymers having the formula

Multibase (Ar Ex)

Multibase contains saturated aliphatic alcohols, polyhydric alcohols, lauric acid esters, petrolatum, water and an emulsifying agent

Lubriderm (Texas Pharmacal)

Lubriderm contains cholesterol esters of lanolin, mineral oil, sorbitol triethanolamine stearate, cetyl alcohol, butyl para hydroxybenzoate and water

WATER IN OIL BASES

Aquaphor (Duke)

Aquaphor is a hydrophilic, but not water washable, ointment containing 6 parts of a mixture of esters and alcohols of cholesterols isolated from wool fat and 94 parts of petrolatum *When water is added to Aquaphor, a water in oil base is obtained*

Eucerine (Duke)

Eucerine is an emulsion of equal parts of Aquaphor and water, plus a small amount of glycerin to enhance stability in cold climates

Nivea (Duke)

Nivea cream is scented Eucerine

Nivea oil is an emulsion of cholesterol alcohols from wool fat and their boric acid esters in a paraffin base and water 30–60 ml of Nivea oil may be added to the bath tub for bathing when the patient has dry skin

Lanolin

Lanolin is wool fat with 25–30% water Naturally occurring wool fat (anhydrous lanolin) contains cholesterol and isocholesterol esters of the higher fatty acids *For a greasier*

ointments except that pastes do not prevent the removal of water or insensible perspiration to as great an extent Hence incorporated drugs exert a milder action Compared with ointment bases pastes are relatively poor vehicles for penetra tion of an incorporated drug They absorb some fluid from lesions Because of their heavy consistency, pastes when cov ered with dressings provide a protective layer through which it is difficult for the patient to scratch and excoriate his skin

Application Pastes should be spread evenly preferably with a tongue blade either on the skin or on the dressing which is to be applied Then dressings should be put on so as to prevent caking of the paste resulting from evaporation of water and to protect against scratching when pruritus is present A suitable dressing consists of one layer of soft linen covered by wrappings of gauze or elastic bandages The dressing should be changed in 24 or 48 hours Cotton saturated with mineral or vegetable oil can be used to remove the paste Water is not effective Care should be taken not to traumatize the underlying skin It is neither necessary nor desirable to remove all the paste in cleansing The purpose of cleansing is to keep the paste from becoming too thick with repeated applications

Pigmenting and Depigmenting Agents

THE COLOR OF A MELANOCYTE depends largely on (1) the amount of melanin in the cell (2) the state of dispersion of the melanin granules in the melanocyte Experimentally many substances can lighten and darken melanocytes However from a practical standpoint at present only one agent monobenzyl ether of hydroquinone is used to depigment skin And one agent 8-methoxypsoralen is used in conjunction with ultraviolet light to repigment skin of patients with vitiligo Both these substances have limitations For example monobenzyl ether of hydroquinone is a potent sensitizer and is not always effective 8 Methoxy

$HOCH_2(CH_2OCH_2)_n CH_2OH$ The number after the Carbowax or polyethylene glycol indicates its approximate molecular weight. Polyethylene glycols range in molecular weight from 200 to 700 and are liquids Carbowaxes range in molecular weight from 1,000 to 6,000 and are solids The lower the molecular weight, the less the viscosity of the polyethylene glycol and the lower the melting point of the Carbowax The consistency of the ointment preparation may be varied by altering the ratio of the ingredients

Plastibase (Squibb)

Plastibase contains 95% heavy mineral oil and 5% poly ethylene plastic resin The mineral oil is dispersed in a matrix of submicroscopic interstices produced from the plastic.

Mineral Oil

Mineral oil, or liquid petrolatum is a mixture of liquid hydrocarbons obtained from petroleum

Paste

The term *paste* is not well defined Older concepts held that a paste was a mixture of 50% powder and 50% ointment Nowa days many pastes contain 20–30% powder instead of 50%

Zinc Oxide or Lassar's Zinc Paste

Zinc Oxide	25%
Starch	25%
White petrolatum	50%

Lassar's original zinc paste was not the formula given here but differed chiefly in that it contained 2% salicylic acid

Indication In general pastes are not used as frequently as oint ments because of difficulty in applying and removing them They are not as attractive cosmetically and in addition require bandaging However, pastes are good therapeutic agents when used properly and are believed by some to be better than oint ments Pastes adhere well to the skin and do not interfere appreciably with perspiration

Mode of action The action of pastes is similar to that of W/O

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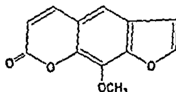
Application Pastes should be spread evenly preferably with a tongue blade either on the skin or on the dressing which is to be applied Then dressings should be put on so as to prevent caking of the paste resulting from evaporation of water and to protect against scratching when pruritus is present A suitable dressing consists of one layer of soft linen covered by wrappings of gauze or elastic bandages The dressing should be changed in 24 or 48 hours Cotton saturated with mineral or vegetable oil can be used to remove the paste Water is not effective Care should be taken not to traumatize the underlying skin It is neither necessary nor desirable to remove all the paste in cleansing The purpose of cleansing is to keep the paste from becoming too thick with repeated applications

Pigmenting and Depigmenting Agents

THE COLOR OF A MELANOCYTE depends largely on (1) the amount of melanin in the cell (2) the state of dispersion of the melanin granules in the melanocyte Experimentally many substances can lighten and darken melanocytes However from a practical standpoint at present only one agent monobenzyl ether of hydroquinone is used to depigment skin And one agent 8-methoxypsoralen is used in conjunction with ultraviolet light to repigment skin of patients with vitiligo Both these substances have limitations For example monobenzyl ether of hydroquinone is a potent sensitizer and is not always effective 8-Methoxy

psoralen plus ultraviolet light is not useful in all patients with vitiligo

Methoxsalen (Oxsoralen, Elder Meloxine, Upjohn)



8 Methoxypsoralen
(8 MOP, methoxsalen Oxsoralen Meloxine)

Mode of action Some aspects of the mechanism of action of the psoralens were discussed in the section on Light Protective Agents The process by which the psoralens in conjunction with sunlight produce repigmentation in vitiligo is not known Recent experiments on vitiligo suggest that the depigmentation is due to the release of a substance like melatonin at the peripheral nerve endings which in turn can cause lightening in color of pigment cells It is possible that psoralens plus sunlight destroy the vitiligo producing agent and allow for subsequent repigmentation

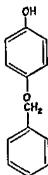
Administration 10–20 mg of 8 MOP is ingested 1 to 3 hours before exposure to sunlight or ultraviolet light from a lamp Since 8 MOP is ineffective unless its ingestion is followed by exposure of the skin to ultraviolet light, the drug should not be given unless light exposure is possible (See section on Light Protective Agents for sun exposure guide to initiate therapy) The exposure time to ultraviolet light should be increased as rapidly as possible without developing excessive erythema Treatment should be continued for at least 3 months Exposure to sunlight is better than exposure to light from an artificial source At times the patients complain of dryness of the skin A bland lubricating ointment is usually effective in alleviating this condition

Not all areas of vitiligo repigment with equal facility As a rule, fleshy areas such as the arm neck and face, repigment better than bony prominences such as the backs of the hands,

bows and knees Some physicians have the impression that epigmentation takes place more readily in children than in dults and that patches of vitiligo of less than 2 years duration epigment better than older lesions The physician should make n effort to use 8-methoxypsoralen and ultraviolet light in the reatment of only a select group of patients with vitiligo The patient must be conscientiously able to follow long term treat nent and in a position to obtain adequate exposure to sunlight or at least 3 months of the year

Many patients seek therapy at a time when the vitiligo is xtending rapidly In these individuals exposure to sunlight may cause an apparent spread of the disease by making visible previ ously unknown areas of vitiligo After maximum repigmentation has been obtained during 3 months of therapy in the summer some patients are instructed to hold off further treatment until spring thus allowing the skin to lighten during the winter

Benoquin (Elder)



Benoquin
(Monobenzyl ether of hydroquinone)

Indication Benoquin is used in treatment of hyperpigmenta tion due to increased melanin such as that in postinflam matory states freckles generalized lentigines berloque dermatitis melasma (chloasma) of pregnancy Addison s disease and chronic malnutrition (Riehl) It is useful to

depigment the remaining areas of normal pigmentation in patients with vitiligo when prospects for repigmentation are not good Benoquin is of little value in the treatment of cafe au lait spots and pigmented nevi It is not effective in malignant melanomas Mild freckling should not be treated, because the incidence of sensitization to Benoquin is high, being 13% Benoquin should not be used in deeply pigmented persons, such as Negroes, because areas of leukoderma may form Such depigmentation is not always reversible

Mode of action Benoquin does not affect the enzymic formation of melanin, but some of its breakdown products may do so It has been suggested that hydroquinone is formed from Benoquin in the skin and that this is the agent which inhibits melanin formation

Application The ointment should be applied 1 to 2 times daily to areas of hyperpigmentation Depigmentation is usually observed after 1 to 6 months of therapy If a sensitization reaction develops, the 20% ointment may be diluted with an O/W base to 5% and applied once daily or less often The 5% ointment although effective, requires a longer time for therapeutic effect than the 20% concentration

Available as Benoquin ointment, 20% concentration in a water washable base in 1¼ oz tubes, and as Benoquin lotion, 5% concentration, in 4 oz bottles

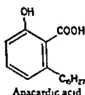
Poison Ivy Hyposensitization

THE PHYSICIAN IS frequently asked about prophylactic desensitization to poison ivy, oak, sumac, etc A highly sensitive person cannot be completely desensitized to poison ivy leaves by conservative oral prophylaxis However some degree of hyposensitization can be achieved The protection is partial Various claims have been made for several oral and injectable products for hyposensitization In general, hyposensitization is not a worth

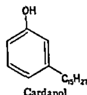
while procedure for most patients with poison ivy however, for those persons who develop a severe contact dermatitis from these plants oral hyposensitization should be attempted The benefits are (1) a briefer course (2) less dissemination and (3) reduced dermatitis The last two are dependent on exposure and original sensitivity None of the preparations described below should be given for the treatment of active poison ivy dermatitis Treat ment should begin during the month of February

Cashew Nut Shell Oil (Method of Kligman)

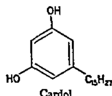
Cashew nuts are obtained from the cashew tree Anacar dium occidentale which is related immunologically to other members of the dermatitis producing family Anacardiaceae such as poison ivy (Rhus radicans), poison oak (Rhus toxico-dendron) the Japanese lac tree (Rhus verniciflua), etc Cashew nut shells contains about 35% oil which can be re leased by heating the nuts Three groups of allergens present in this oil are (1) anacardic acid (2) cardanol and (3) cardol



Anacardic acid



Cardanol



Cardol

Each of these agents is a mixture of four substances having different degrees of unsaturation in the side chains The sub stances are structurally similar to allergens obtained from poison ivy Cashew nut shell oil* to be used for hyposensitiza tion should have an iodine number of over 250 It is washed with weak sulfuric acid to remove mineral salts and amines The washed shell oil is prepared for use as follows

Cashew nut shell oil	10 0
Aerosol OT (American Cyanamid)	2.5
Tenox II (Eastman Kodak)	0 1
Ethyl alcohol	90 0

* Cashew nut shell oil can be obtained from the Irvington Chemical Division of the Minnesota Mining and Manufacturing Co Newark 5 N J

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1 50 dilution First week	½ the maximum number of drops ingested when bottle of 1 100 dilution was exhausted
Second and following weeks	Increase the daily number of drops as rapidly as tolerance permits until 1 50 dilution is completed
1 25 dilution First week	½ the maximum daily dose of previous concentration Increase dosage as tolerance permits until 1 25 dilution is completed

A maintenance dose of 1 capsule (12 drops) of 1 25 dilution of oleoresin should be taken 2 or 3 times weekly Side reactions include pruritus and generalized pruritus erythematous eruptions etc

Available in a treatment set consisting of three 15 ml bottles of oleoresin in the following dilutions 1 100 1 50 and 1 25 Gelatin capsules are provided which can be filled with the requisite amount of oleoresin oil from the dropper bottle for ingestion

Oleoresin in Alcohol (Milderm Research)

This preparation is an extract of poison ivy leaves and stems in 70% ethyl alcohol

Dose 5 drops in ¼ glass of water milk or fruit juice for 6 weeks before the poison ivy season then 3 times a week during the season

Protective Ointments Against Water and Oil

MANY PREPARATIONS ARE available to protect the skin against water and oil Plain petrolatum is more effective than many more expensive products The addition of silicones to petrolatum

Aerosol OT is a wetting agent Tenox II is an antioxidant

DOSAGE PLAN

First week	1 drop daily
Second week	2 drops daily
Third week	3 drops daily
Fourth week	4 drops daily thereafter increase by 1 drop every 4 days to a total of 20 drops daily continue at this final dose until a total of 35 ml has been taken

The drops are added to a full glass of warm water or other liquid, stirred and drunk with a glass or disposable straw The oil forms a milky emulsion in water The water should not be ice cold, lest the emulsion break After the first week the daily dose is split into a morning and evening portion as this division lessens side reactions The liquid should not touch the glabrous skin The most common side reactions are skin eruptions of a pruritic, erythematous type and mild stomatitis The drops should be stopped in the presence of pruritus or a rash and then resumed more slowly Four months is the average course Hyposensitization is temporary as the effects begin to wane in about 6 weeks A spring course ending in early summer generally provides suitable protection for the remainder of the season Treatment has to be repeated each year, or hyposensitivity may be perennially maintained by taking 5 drops of 10% cashew oil daily

Oleoresin in Corn Oil (Hugh Graham Inc)

Oleoresins are available in corn oil for ingestion to reduce sensitivity to contact with poison ivy and other plants The required amount of oil can be ingested in from 1 to 4 months Rapidity of increasing dosage depends on individual tolerance

DOSAGE PLAN

1 100 dilution	
First week	1 drop daily
Second week	2 drops daily
Third and following weeks	Increase daily number of drops as rapidly as tolerance permits until contents of 15 ml bottle of 1 100 dilution have been ingested

feeling This is one of the reasons they are mixed with other substances before being put on the skin We have found that the pure dimethyl siloxane polymer of 1 000 centistoke viscosity is an ideal liquid to use for protective purposes This liquid can be purchased from Dow Corning or General Electric

Domecone (Dome)

Dimethyl siloxane of 1 000 centistoke viscosity	20%
Water washable base	80%

OTHER PROTECTIVE AGENTS

Tecto (Duke)

This preparation consists of Eucerine with the addition of paraffin wax as a stiffening agent No perfumes are present *Available* in 120 Gm tubes and 1 lb jars

Kerodex (Ayerst)

Two preparations are available Kerodex 51 for dry work Kerodex 71 for wet work Neither contains silicone They are made of mixtures of zinc stearate and oxide kaolin magnesium silicate fullers earth cholesterol alcohols and esters petrolatum and other substances
Available in 4 oz tubes

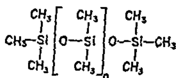
Psoriasis Preparations

PSORIASIS IS A METABOLIC DISEASE of the skin in which the specific biochemical defect is unknown However there are 2 interesting points that may shed light on its etiology Substances which combine with or inactivate sulfhydryl groups tend to bring about a remission e g radiant energy heavy metals and organic oxidizing compounds. Even though this association does not establish

paraffin oil, castor oil, etc, enhances the resistance of these substances to solvents

SILICONES

Silicones provide a chemically inert film to protect the skin against water and chemicals They are of particular value in soap and water dermatitis, diaper rash, decubitus ulcers, areas surrounding colostomy openings, etc The silicones are less effective against oils and solvents They are not miscible with water They possess much of the stability of glass, quartz and the mineral silicates, to which they are related chemically The skin should be clean and dry before use of silicones A thin film of the preparation should be applied to the skin before exposure to fluids.



Polymers of dimethyl siloxane units
(Dow Corning 200 fluids)

The average length of the chain determines the viscosity of the fluid the longer the polymer, the more viscous the silicone

Silicote Ointment *(Arnar Stone)*

Dimethyl siloxane of 60 000 centistoke viscosity	30%
White petrolatum	70%

Available in 60 Gm tubes and 1 lb jars

Silicote Liquid Spray *(Arnar Stone)*

Dimethyl siloxane of 350 centistoke viscosity In a petrolatum base with Freon propellent	33⅓%

Available in 3 oz cans

Liquid Silicone

The dimethyl siloxane polymers vary in viscosity depending on the length of the chain Most pure silicones have a tacky

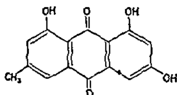
3 Ammoniated mercury 5%
Salicylic acid 2%
In a washable or petrolatum base
HgNH Cl

Ammoniated mercury (mercury amino chloride)
Available on prescription

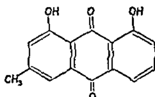
4 Ammoniated mercury 10%
Salicylic acid 5%
Phenol 5%
In a washable or petrolatum base
Available on prescription

5 Salicylic acid 1–5%
In a washable or petrolatum base
Available on prescription

6 Chrysarobin 0 25–2 0%
In petrolatum or as solution in flexible collodion
Chrysarobin is a mixture of substances from Goa powder which includes emodin chrysophanic acid and their derivatives Quinones of these types are ordinarily effective sulfhydryl binding agents
Available on prescription.

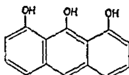


Emodin



Chrysophanic acid

7 Anthralin 0 1–0 5%
In petrolatum or as solution in flexible collodion
Anthralin is related in structure to emodin and *chrysophanic acid which are found in chrysarobin*



Anthralin

Available on prescription.

an etiologic relationship between the metabolism of sulfhydryl containing compounds and psoriasis, it is a point to remember A second interesting point is that light makes lupus erythematosus worse, but chloroquine improves it The reverse is true for psoriasis—light improves psoriasis and chloroquine makes it worse.

In this section are commonly used preparations containing tar, salicylic acid, mercury, phenol, etc In addition, information is given regarding ACTH, triamcinolone, aminopterin, methotrexate and nitrogen mustard

The various tar preparations contain polyphenolic substances and peroxides which might inactivate epidermal sulfhydryl groups. Thus their effect on skin is similar to that produced by exposure to radiant energy The effect of tar is enhanced when skin to which tar has been applied is exposed to ultraviolet light Ultraviolet light seems to potentiate the oxidizing properties of tar

Mercury usually is made available in the form of ammoniated mercury and mercuric salts of fatty acids Even though mercury compounds are very sensitizing, they are useful because of their pronounced therapeutic value It is possible that these mercuric compounds are effective because they combine with sulfhydryl groups in the skin

Salicylic acid is a keratolytic agent and hence is useful in the removal of scales from psoriatic patches Through some unknown mechanism it also promotes normal keratin formation

The actions of phenol, cresol anthralin and chrysarobin are unknown Whether allantoin has a beneficial effect on psoriasis remains to be seen

SKIN CARE

Ten Common Agents for Psoriasis of the Glabrous Skin

1 Tar 3%
Salicylic acid 5%
In petrolatum base
The salicylic acid concentration may be varied from 1 to 5% and the tar from 1 to 5%
Available on prescription

2 Liquor carbonis detergens full strength
Available in 3, 8 and 16 oz bottles and in a 2 oz aerosol spray

Tar and Ultraviolet Light Procedure

1. In the morning rub thin layer of tar ointment into involved skin areas If the tar layer is thick ultraviolet light will not penetrate to the epidermal cells
2. Expose skin to ultraviolet light (See section on Ultraviolet Light for exposure schedule)
3. One hour (or more) after ultraviolet light exposure bathe and rub scaly lesions vigorously with a brush and some cleaning agent
4. After bathing rub ample amount of tar into involved areas
5. Reapply tar liberally at bedtime
   Repeat above procedure daily and increase the intensity of light striking the skin daily

Systemic Agents

ACTH

Injection of ACTH usually results in improvement in psoriatic lesions This therapy is not practical for routine use because daily injections are required and serious side effects occur with prolonged therapy (See section on Steroids and ACTH)

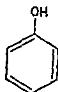
Triamcinolone (Aristocort Kenacort)

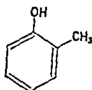
Like ACTH triamcinolone in sufficient doses can bring about clearing of lesions in most psoriatic patients This effect is observed less frequently with the other steroids If the patient responds to an initial dose of no more than 32 mg of triamcinolone and if the maintenance dose is 4–8 mg daily this steroid can be used in management of some patients Unfortunately most require a daily maintenance dose of more than 8 mg With prolonged therapy even in small doses triamcinolone produces weight loss and moon facies When therapy is discontinued psoriatic lesions may recur (See section on Steroids and ACTH)

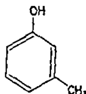
8 Riasol (Shield)

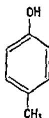
Mercury soaps $(RCOO)_2Hg$	0 45%
Phenol	0 5 %
Cresol	0 75%

In a lotion base









Phenol

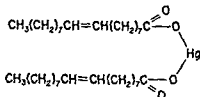
Cresol

Available in 4 and 8 oz bottles

9 Siroil (Siroil)

Mercuric oleate	0 4%
Cresol	

In a lotion base



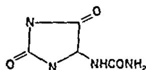
Mercuric oleate

Available in 8 oz bottles

10 Alphosyl (Reed and Carnrick)

Allantoin	2%
Coal tar extract	5%

In lotion form



Allantoin

Allantoin is a product of purine metabolism

Available in 8 oz bottles

reactions It is not known how Aminopterin exerts its beneficial effects in psoriasis It is possible that folinic acid is needed for the formation of keratin proteins and that Aminopterin interferes with the keratinizing process

Dose One 0 5 mg tablet by mouth daily not exceeding 6 mg total dose in a period of 12–20 days A common schedule would be 1 tablet daily for 6 days followed by 1 week s rest and then 1 tablet daily for another 6 days Or the patient could be given 1 tablet daily for 12 days The white count should be checked weekly

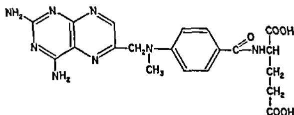
Available in 0 5 mg tablets

Side effects Toxic reactions occur in 10% of the patients Toxic effects coincide with improvement of psoriasis and include ulceration of the buccal mucosa, diarrhea abdominal cramps alopecia decrease in need for shaving and delay in wound healing

Antidote Folinic acid (leucovorin) may be used to counteract inadvertent overdosage of Aminopterin

Dose 1–2 ml (3–6 mg) intramuscularly given immediately May not be effective if given more than 4 hours after folic acid antagonists

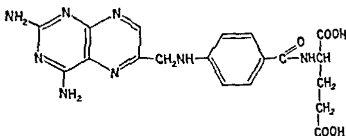
Methotrexate (Lederle)



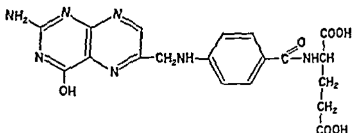
Methotrexate
(4 Amino-N[10] methyl pteroylglutamic acid)

This folic acid antagonist is related to Aminopterin in structure Although it is given in 5 times the concentration of Aminopterin its toxic reactions are less

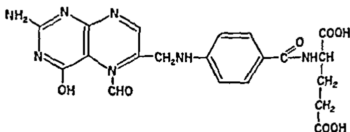
Aminopterin (Lederle)



Aminopterin
(4 aminopteroylglutamic acid)



Folic acid



Folinic acid

Comparing the structural formulas of folic acid and Aminopterin reveals an OH group on one of the rings in *folic acid* and an NH_2 group at this same site in Aminopterin Folic acid is converted to folinic acid (citrovorum factor), which participates in several biochemical reactions Aminopterin competes with folic acid to prevent its conversion to *folinic* acid, and it also competes with folinic acid in its biochemical

reactions It is not known how Aminopterin exerts its beneficial effects in psoriasis It is possible that *folinic acid* is needed for the formation of keratin proteins and that Aminopterin interferes with the keratinizing process

Dose One 0.5 mg tablet by mouth daily, not exceeding 6 mg total dose in a period of 12–20 days A common schedule would be 1 tablet daily for 6 days followed by 1 week's rest and then 1 tablet daily for another 6 days Or the patient could be given 1 tablet daily for 12 days The white count should be checked weekly

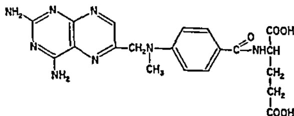
Available in 0.5 mg tablets

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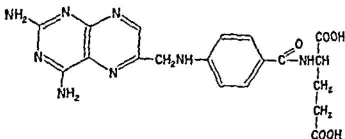
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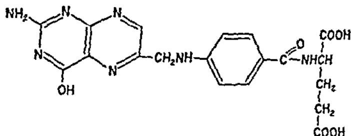
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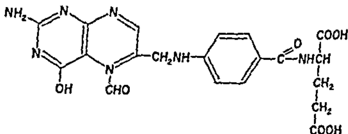
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NAIL CARE

Mercury

Ammoniated mercury 20%
In a washable base

Apply to the nails twice daily
Available on prescription

Gelatin

The use of gelatin as outlined in the treatment of brittle nails is of questionable value in psoriasis

X Ray

The dorsal surface of the entire hand or just the fingers may be treated with 100 kv 2 mm aluminum for a total dose of 220 r This can be repeated once after 1 month DO NOT REPEAT THEREAFTER

Rosacea Preparations

MANY AGENTS USED for the treatment of common acne are helpful in rosacea These include lotia alba salicylic acid resorcinol alcohol etc (See section on Acne Preparations) In addition the following ointments available on prescription, are used to treat rosacea They should be applied nightly Their mode of action is not known

Sulfur Sal Quinoline Ointment

Sulfur 1%
Salicylic acid 1%
In Quinolor Vioform or Sterosan ointment

Dose Follow the schedule given for Aminopterin, substituting a 2 5 mg tablet of Methotrexate for 0 5 mg Aminopterin
Available in 2 5 mg tablets

Nitrogen Mustard

It is possible that nitrogen mustard may be of benefit However, this drug should be used only in the exceptional patient with extensive and refractory psoriasis (See section on Nitrogen Mustard Therapy)

SCALP CARE

Care of the scalp consists in the application of tar, mercury and phenol products as well as ultraviolet light irradiation (See section on Ultraviolet Light) At bedtime one of the following preparations should be rubbed into the scalp thoroughly and allowed to remain during the night The next day the scalp may be washed and brush scrubbed with tincture of green soap or other shampoo This treatment should be carried out daily for 2 to 3 days and then twice weekly

Tar Mercury Ointment

Ammoniated mercury	3–12%
Salicylic acid	1– 5%
Coal tar (Zetar Almay LCD)	2–10%
In a water washable base	

Mercury may be omitted when patients are sensitive to this metal
Available on prescription

Pragmatar (Smith Kline & French)

See section on Seborrheic Dermatitis Preparations

P & S Liquid (Baker)

Phenol	1%
Saline	

Available in 4 and 8 oz bottles

Seborrheic Dermatitis Preparations

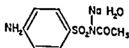
THE OLD STANDBYS FOR treating seborrheic dermatitis namely sulfur tar and ammoniated mercury are being replaced by drugs which are not only more effective but also more acceptable to the patient from a cosmetic standpoint. Nevertheless the older compounds are still useful It is of interest that different types of agents are valuable in treating seborrheic dermatitis steroids chemotherapeutic drugs sulfur tar and ammoniated mercury Combinations of these substances are available For the treatment of acute extensive seborrheic dermatitis systemic therapy with steroids or ACTH should be given The preparations below suggested for treatment of seborrheic dermatitis of the skin should be applied 2 to 3 times daily For treatment of the scalp Sebizon Pragmatar etc are applied at bedtime in ordinary cases and during the day as well in severe cases

Hydrocortisone Derivatives

Steroids in lotion or ointment form are often effective in the treatment of seborrheic dermatitis (See section on Steroids and ACTH)

Sebizon (Schering)

Sodium sulfacetamide with a wetting agent in a lotion bas of poly ethylene glycol esters to prevent crystalliza tion of the sodium sulfacetamide on the hair	10%



Sodium sulfacetamide

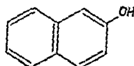
Caution Contact dermatitis to sodium sulfacetamide some times occurs

Available in 3 oz plastic squeeze tubes

Beta Naphthol Ointment

Beta naphthol	0 55%
Sublimed sulfur	1 1 %

In equal parts balsam of Peru and petrolatum



β Naphthol

Sublimed sulfur is obtained directly through the sublimation of crude sulfur Balsam of Peru is a liquid obtained from Myroxylon pereirae It contains 50–60% cinnamein a volatile oil to which its therapeutic properties are attributed Cinnamein consists of the esters of benzoic and cinnamic acids There is 28% resin, styracin and vanillin

In the past, when rosacea was thought due to Demodex folliculorum, this formula a known scabicide, was proposed to see whether it would work as destructively on Demodex as on Acarus scabiei Although the Demodex etiology of rosacea *has not been substantiated, this formula has been retained for treatment of rosacea because of its therapeutic effectiveness*

Application Rub onto face nightly A burning sensation is to be expected Observe patient the day following every third application because of possible occurrence of dermatitis

Darier's Paste

Precipitated sulfur	6 0 Gm
Resorcinol	2 0 Gm
Zinc oxide	8 0 Gm
Starch	8 0 Gm
Yellow petrolatum	10 0 Gm
Lanolin	10 0 Gm

Soaps, Shampoos and Baths

SOAPS

SOAPS EMULSIFY FATS with water and help remove dirt particles from the skin In dermatologic disorders it is important to clean the skin It also is important how this cleaning is done Ordinary soap has the shortcoming of being made up of sodium or potassium salts of fatty acids produced by neutralizing weak organic acids with a strong base Such a soap hydrolizes in water to produce a definitely alkaline pH Solutions at alkaline pH are good protein solvents and tend to dissolve keratin In many dermatologic disorders the skin already is more alkaline than under normal conditions Therefore adding ordinary soap to damaged skin may keep a vicious circle going

When a patient says that he is sensitive to soap he does not usually mean that there is an acute allergic reaction but rather that certain physical properties—such as high pH and cleansing action—tend to irritate and damage his skin This situation pertains to most patients with eczematous eruptions To correct this problem and to get a cleansing agent that can be tolerated by these patients one must find a soap that is at a neutral or acid pH Another approach would be to use a less efficient alkaline soap such as a superfatted one

NEUTRAL SOAPS AND SOAP SUBSTITUTES

As mentioned before soaps are ordinarily sodium or potassium salts of fatty acids These salts of strong bases and weak acids hydrolyze in water to form solutions at a pH of 9 to 10 To obtain a soap of greater neutrality or acidity salts must be prepared by combining strong or weak bases with strong acids or by combining weak bases with weak acids. Most neutral soaps and soap substitutes (Dove Lowila Dermolate pHisoderm and Soy Dome) consist of long chain esters with a sulfate salt at the end of the molecule. These sulfate salts are derived from strong acids They

Metimyd Ointment with Neomycin (Schering)

Sodium sulfacetamide	10 %
Prednisolone	0 5 %
Neomycin sulfate	0 25%

In a petrolatum type base

Available in 1/8 oz applicator tube

Pragmatar (Smith, Kline & French)

Cetyl alcohol coal tar distillate	4%
Micronized sulfur	3%
Salicylic acid	3%

In oil in water emulsion base

Available in 1½ oz jars

Sulfur Ointment

Precipitated sulfur	2–10%
Salicylic acid	1– 2%
Tar	2%

In an ointment base

Available on prescription

Ammoniated Mercury Ointment

Ammoniated mercury	5%
Salicylic acid	1–2%

In an ointment base

Available on prescription

Antibiotic Ointments

Bacitracin
Neopolycin
Neosporin
Spectrocin

These antibiotics are available with or without steroids (See the section on Chemotherapeutic Drugs)

Soaps and Shampoos

In seborrheic dermatitis, these soaps and shampoos are often helpful They are described in the following section on Soaps, Shampoos and Baths

Soaps	Shampoos
Acne Aid	Capsebon
Fostex (bar or cream)	*Duponal*
Sulpho Lac (bar or cream)	Sebulex
Tar soap	Selsun
	Tincture of green soap

Soaps, Shampoos and Baths

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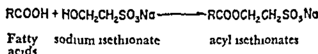
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dissociate in water to give a pH of about 7 in the case of sodium sulfates and of less than 6 in the case of ammonium sulfates The degree of dissociation of sulfate soaps is greater than that of ordinary soaps

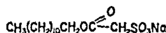
Dove Soap (Lever)

This bar consists of an anionic detergent, a fatty acid emollient, plasticizer and perfume The anionic detergent is an acyl isethionate made by condensing fatty acids with sodium isethionate The pH is 7

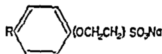


Lowila (Westwood)

Available as a bar or liquid, Lowila contains sodium lauryl sulfoacetate in a corn dextrin base acidified with lactic acid The pH in solution is 4 0 Lowila liquid, used for washing dishes laundry, etc , contains an alkyl aryl sulfonate acidified with lactic acid to a pH of 4 0–4 5



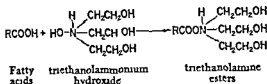
Sodium lauryl sulfoacetate



Alkyl aryl sulfonate

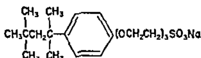
Neutrogena (Natone)

This bar is made by combining fatty acids with triethanolamine Added glycerin makes the soap transparent It is claimed that solutions of this soap have a pH of 7 5 However 1% solutions we tested had a pH of 9 5



pHisoderm (Winthrop)

This is a stable emulsion of sodium p terocytyl phenoxy ethoxyethoxy ethyl ether sulfonate petrolatum lanolin cholesterols and water and is free from alkalis and fatty acids It has a pH of 5 5 It comes in three forms regular for normal skin oily for dry skin and ichthyosis and dry for oily skin



Sodium p-terocytyl phenoxy-ethoxyethoxy ethyl ether sulfonate

Dermolate (White)

Dermolate is a lathering cake detergent made from fatty acids by first methylating and then sulfating refined tallow It has a pH of 8 4 and consists of

Sodium sulfato-octadecanoate	38%
Sulfato-octadecanoic acid	7%
Sodium stearate	38%
Perfume	0 075%
Water	9%



Sodium sulfato-octadecanoate



Sulfato-octadecanoic acid

Acidolate (White)

Acidolate is a nonlathering liquid skin detergent with a pH of 6 4 It is composed of

Sulfated rice bran oil	26.5%
Light mineral oil	20 5%
Water	53 0%

Aveeno Soap Substitute (Aveeno)

This product, a powder, consists of 65% Aveeno colloidal oatmeal in a petrolatum base It contains no soap or wetting agent The pH is approximately 6 0

Soy Dome Soapless Cleanser (Dome)

Available as a cream, Soy Dome contains 10% soya flour, which is the meal of defatted and dehulled soy beans The dry flour contains approximately 55% protein and is standardized to a particle size of 75 microns Foaming and cleansing action are dependent on ammonium lauryl sulfate Some ammonium myristyl sulfate is also present The pH is 5


$CH_3(CH_2)_{11}OSO_3NH_4$

Ammonium lauryl sulfate


$CH_3(CH_2)_{13}OSO_3NH_4$

Ammonium myristyl sulfate

SUPERFATTED SOAPS

Superfatted soaps contain added fat or oil for the purpose of preventing excessive defatting of dry skin Such soaps probably are less drying than ordinary ones because their detergent properties are less The better a detergent, the more defatting it is Consequently, adding a fat to a detergent will not decrease the defatting properties of the detergent unless it makes it a less effective cleansing agent Nevertheless, soaps that suds well and yet probably have reduced detergent action are useful for patients with dry skin

Basis Soap (Duke)

This is a bar containing 2% of a mixture of cholesterol esters of lanolin and wool fat

Oilatum Soap (Stiefel)

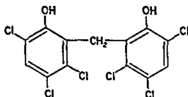
This lanolin free bar contains 7 5% peanut oil and is available scented or unscented

Superfatted Soap (Stiefel)

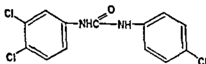
This bar contains 6% lanolin

Germistatic Soaps

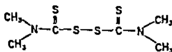
Soaps with bacteriostatic agents have become increasingly pop ular for 2 reasons First they have been recommended as an adjunct to the treatment of pyogenic skin infections Infections with staphylococcal antibiotic resistant organisms have become a severe medical problem Cleaning agents that will reduce the likelihood of a staphylococcal skin infection are sought and widely used Second these soaps are promoted as deodorants In this regard they are effective because they inhibit organisms respon sible for the production of odor in body folds Most of the germistatic soaps are effective against gram positive organisms Their activity against gram negative organisms is low Bacterio stats commonly added to soaps are hexachlorophene (G 11) trichlorocarbanilide (TCC) and tetramethyl thiuram disulfide (TMTD)



G-11
(Hexachlorophene)



TCC
(3 4 4 Trichlorocarbanilide)



TMTD
(Tetramethyl thiuram disulfide)

Dial Soap (Armour)

Initially, Dial soap contained 2% G-11 The present Dial soap contains 0 5% G 11 and 0 5% TCC G 11 and TCC are a synergistic combination, and this mixture is more bacteriostatic than 2% G 11 It is formulated from the sodium salts of various fatty acids and has a pH of 9 7

Zest (Proctor and Gamble) **Lifebuoy** (Lever) **Praise** (Lever)

The large soap manufacturers are now promoting soaps with bacteriostatic agents The active agents have been changed from time to time It has not been possible to obtain detailed information on the compounds used today For example Lifebuoy originally contained cresol In 1953 the cresol was replaced by TMTD which in turn was replaced recently by another agent The present Zest product contains TCC

pHisoHex (Winthrop)

This liquid soap is the same as pHisoderm but with 3% G 11 added It has a pH of 5 5
Available in 5 and 16 oz bottles

Septisol (Vestal)

This liquid soap contains 0 75% G 11 or 2% G 11 based on soap content

SOAPS AND SHAMPOOS FOR ACNE AND/OR SEBORRHEA

Acne Aid (Stiefel)

Sulfated vegetable oil	10 5%
Neutral soap	89 5%

Fostex (Westwood)

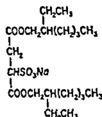
This cleansing agent contains keratolytic and drying agents

Sebulytic (sodium dioctyl sulfosuccinate sodium lauryl sulfoacetate so-

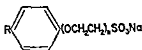
dium alkyl aryl polyether sulfonate)

Micropulverized sulfur	2%
Salicylic acid	2%
Hexachlorophene (G-11)	1%

In a corn dextrin base



Sodium dioctyl sulfosuccinate



Sodium alkyl aryl polyether sulfonate

Available as a cream in 4½ oz jars and as a bar

Sulpho-Lac (Kelgy)

This bar contains 10% colloidal sulfur in a soap made from coconut oil and white tallow

Tar Soap (Packers)

This soap contains 6% pine tar in a toilet soap base It is recommended by some for use in place of ordinary cleansing soap *in the presence of seborrhea seborrheic dermatitis and* psoriasis.

Capsebon (Pitman-Moore)

Capsebon is a suspension of 1% cadmium sulfide in a detergent base made up of triethanolamine lauryl sulfate and lauric acid diethanolamine condensate

CdS
Cadmium sulfide

Available in 4 oz. bottles.

Sebulex (Westwood)

This is a keratolytic shampoo which contains the same ingredients as Fostex cake and cream but is less drying because

Dial Soap (Armour)

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Dial Shampoo (Armour)

This liquid contains 1% hexachlorophene (G 11), 25% triethanolamine lauryl sulfate lanolin derivatives and water
Available in 3½ and 7 oz bottles

BATHS

For a therapeutic bath the tub should be filled half full In the average home bathtub 75 liters (20 gal) of water will be adequate for this purpose Full length hospital tubs may require 2 to 3 times this amount For a sitz bath 20–30 liters (5–8 gal) of water will suffice in either home or hospital tub The temperature of the water should be approximately 95–100° F (35–38° C) The patient may be allowed to remain in the tub ½ hour Debilitated patients should be watched carefully At times it may be necessary to have the patient rest in a canvas sling suspended in the tub The patient should be instructed to dry himself by patting gently with soft towels rather than by rubbing

Colloid Baths

Colloid baths consist of proteins or starch in water and are used for their soothing and antipruritic effect The mechanism of this action is not known

1 *Aveeno* is a finely milled oatmeal preparation containing 24% protein 9% oil and 46% starch To minimize lumping shake 1 cup of Aveeno and 2 cups of cold water in a quart jar Pour mixture into bath For infants use only 3 to 5 heaping tablespoonfuls of Aveeno
Available in 18 oz and 4 lb boxes
2 *Aveeno Oilated* consists of regular Aveeno oatmeal plus 35% of a mixture made up of liquid petrolatum and lanolin derivatives This preparation is indicated for patients with dry skin when an emollient effect is needed
Available in 10 oz. cans
3 *Soyaloid Colloid Bath* (Dome) contains 52% protein from soy beans.
Available in boxes containing five 3 oz packages

of the addition of a dewaxed oil soluble fraction of lanolin. *Available* in 4 oz. bottles.

Selsun (Abbott)

This shampoo is a suspension which contains a detergent and 2.5% of a mixture of crystalline selenium monosulfide and solid solutions of selenium and sulfur in an amorphous form, part of which could have the formula Se S_m, where $n+m=8$. Selenium sulfide is made up of 2 elements which have some similar chemical properties and which occur adjacent to one another in the same group of the periodic table.



Available in 4 oz. bottles.

Soft Soap (U.S.P.)

Soft soap (green soap, medicinal soft soap, sapo mollis) is a potassium soap made by the saponification of vegetable oils, excluding coconut oil and palm kernel oil, without the removal of glycerin.

Vegetable oil	380.0 Gm
Oleic acid	20.0 Gm
Potassium hydroxide (85% strength)	91.7 Gm
Glycerin	50.0 ml
Distilled water to make	1 000.0 Gm

The vegetable oil may be corn, cottonseed, linseed, olive, soy bean or a similar oil with a saponification value not greater than 205 and an iodine value not less than 80.

Tincture of Green Soap Shampoo (soft soap liniment)

Medicated soft soap (see preceding)	65 Gm
Lavender oil	2 ml
Alcohol to make	100 ml

Adjunct. 2–5% crude coal tar or liquor carbonis detergens may be incorporated in tincture of green soap in the treatment of seborrhea, seborrheic dermatitis or psoriasis.

3 *Gen Bath* (Dermik) is a mixture of vegetable oils having a low index of unsaturation with an emulsifying agent *Available* in 6 oz bottles

Tar Baths

30 ml (1 oz) of a liquid tar preparation (Zetar Almay or LCD) may be added to the bath in cases of pruritus psoriasis and seborrheic dermatitis (See section on Tar Preparations)

Potassium Permanganate ($KMnO_4$) Baths

A potassium permanganate bath is used in infected and weeping dermatoses and bullous eruptions such as pemphigus Potassium permanganate is germicidal drying and deodorizing because of its oxidizing properties The requisite amount of potassium permanganate either crystals or crushed tablets should be dissolved in 1 qt of water which should then be added to the tub The patient should get into the bath immediately so that his skin can benefit from the oxidizing properties of the potassium permanganate

For a 1 10 000 dilution use twenty five 0 3 Gm (5 gr) tablets or 2 tsp of crystals For a 1 20 000 dilution use twelve 0 3 Gm (5 gr) tablets or 1 tsp of crystals When tablets are used they must be finely pulverized between 2 wooden tongue blades

Steroids and ACTH

THE USE OF STEROIDS and antibiotics represents the most important advance in dermatologic therapy of this century The steroids have a pronounced effect on allergic reactions eczemas bullous eruptions and diseases of connective tissue In 1951 cortisone was made available commercially Since then the influx of new steroids has proceeded with unabated rapidity hydro-

4 *Oatmeal and soda* Boil 2 cups of bulk oatmeal in 1 qt of water in a double boiler for 30–45 minutes Or cook 2 cups of quick cooking oatmeal in 1 qt of water for 1 minute Allow to cool for 15 minutes Add ½ cup baking soda ($NaHCO_3$) Pour entire mixture into a gauze bag and tie shut The patient should express the oatmeal mash through the gauze, applying it over the body The mash should be thoroughly washed off before leaving the tub

5 *Cornstarch* Three types of cornstarch are available (1) edible starch, representing raw cornstarch in a powdered form, (2) gloss starch a raw cornstarch in lump form, and (3) Linit, a modified starch, made by subjecting the starch to a mild acid treatment followed by neutralization washings and filtration The product contains approximately 1% boric acid, which is added before drying of the starch Linit is not 'preboiled' and has undergone little hydrolytic degradation of the starch molecule, nevertheless, the physical properties have been changed so that it produces solutions of less viscosity than native cornstarch Mix 2 cups of starch, preferably Linit, with 4 cups of tap water to form paste Add mixture to tub while stirring

6 *Starch and soda* Mix 2 cups of cornstarch and 1 cup of baking soda in a basin of cold water Add mixture to tub bath

Bath Oil

Some believe that addition of oil to the bath water may help prevent drying of dry skin However others believe that it is not possible to wash and lubricate the skin simultaneously, that it is necessary first to wash and then to apply a lubricating preparation

1 *Lubath* (Texas Pharmacal) consists of cottonseed oil made dispersible by incorporation of a nonionic wetting agent, Triton X 45
Available in 8 oz bottles

2 *Alpha Keri* (Westwood) consists of a dewaxed oil soluble lanolin fraction in combination with mineral oil
Available in 8 oz bottles

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dermatitis etc, to prolong life in otherwise fatal cases of disseminated lupus erythematosus pemphigus etc For acute anaphylactic reactions intravenous administration of steroids is not as effective as subcutaneous or intramuscular injection of epinephrine which is the drug of choice or intramuscular injection of antihistamines

Mode of action Steroids decrease tissue reactivity diminish tissue response to antigen antibody reactions and inhibit proliferation of fibroblasts Cortisone is converted to hydrocortisone which is the active agent. The prednisolone and fluorinated derivatives are metabolized at a slower rate than cortisone and hydrocortisone This may be one reason why smaller quantities are required to attain a therapeutic effect A comparison of the effects of steroids and antihistamines on different types of allergic reactions is given in the table

REACTION TYPE	STEROIDS	ANTIHISTAMINES
Anaphylaxis	↓ or 0	↓
Immediate type skin tests	0	↓
Delayed type skin tests	↓	0
Vascular les ons of serum sickness type	↓	0
Allergic encephalomyelitis	↓	0
Antibody formation	↓ or 0	0
Atopic reactions	↓	↓ or 0

↓ = Inhib tio f reactio 0 = N ffect o reactio

A question often asked is whether the various steroids affect the same diseases in the same way or whether certain steroids affect one disease more than another It is likely that some specificity is involved although much more experience will be required to choose correctly the steroid best suited for treatment of a particular disease The polypeptide ACTH and the steroid triamcinolone benefit psoriasis many steroids do not.

Dose Before initiating steroid therapy the physician must know the general medical status of the patient He must rule out by history and/or laboratory examination hypertension diabetes peptic ulcer psychosis and systemic infection such as tuberculosis etc If one or more of these diseases is present the decision as to the use of steroids and the dose will depend on the severity of that disease and the possibility of controlling it For example if mild diabetes mellitus is present which

cortisone, prednisone, prednisolone, fluorohydrocortisone (fludrocortisone), methylprednisolone, triamcinolone, triamcinolone acetonide, dexamethasone, fluorometholone and 6 fluoroprednisolone. Six of these 11 steroids contain fluorine Some steroids are active topically while others are not

SYSTEMIC ADMINISTRATION OF STEROIDS

On a weight basis, cortisone is the least potent of the steroids If cortisone is taken as a reference standard with regard to dermatologic effectiveness, then the amount of hydrocortisone required to produce the same effect would be 0 8 the cortisone dose, prednisone and prednisolone 0 4, methylprednisolone and triamcinolone 0 32, 6 fluoroprednisolone 0 16 and dexamethasone 0 08 These ratios do not apply to nondermatologic disorders such as Addison s disease, arthritis blood dyscrasias etc If 100 mg of cortisone is required to produce a favorable therapeutic response, the dose requirements of the other steroids would be

Cortisone	100 mg
Hydrocortisone	80
Prednisone and prednisolone	40
Methylprednisolone and triamcinolone	32
6 Fluoroprednisolone	16
Dexamethasone	8

Triamcinolone acetonide fluorometholone and fluorohydrocortisone are used topically but not orally Both triamcinolone acetonide and fluorometholone are active orally at a dose level comparable to that of prednisolone However, topically they are potent anti inflammatory agents and are effective in small concentrations For this reason these drugs are sold only for topical application As an anti inflammatory agent, fluorohydrocortisone is approximately 10 times as potent as hydrocortisone However, its salt retaining effects are 50 times greater consequently, it is not used systemically for dermatologic disease

Indication Steroids are used to shorten acute self limited dermatoses, such as severe contact dermatitis drug reactions urticaria and other sudden tissue responses, to control acute exacerbations of chronic disorders such as atopic dermatitis seborrheic

while to give 100 units ACTH gel daily in addition to maintaining the oral steroid dose The clinical impression exists that ACTH preparations have a direct tropic action on the skin in addition to stimulating the production of hydrocortisone by the adrenal gland In patients on high doses of steroids by mouth, the hydrocortisone output by the adrenal gland probably is nil, and this situation is not changed by the administration of ACTH However the direct action of ACTH on the skin may be responsible for the beneficial effect The purified ACTH available commercially contains about 10% ACTH and 90% other materials from the pituitary gland It is not known whether the good effects stem from the ACTH or from one of the other agents present

Side effects A sense of well being is frequently noted by patients under treatment with steroids During prolonged therapy the patient should be observed at regular intervals because complication may occur such as gastrointestinal ulceration, hypertension masking of an intercurrent infection diabetes and thrombophlebitis Acne moon facies hirsutism and ecchymoses may develop but these usually cease on withdrawal of the drug

The following examinations should be carried out periodically blood pressure weight urinalysis white blood cell count The diet should be high in protein to help maintain body stores of calcium and to counteract protein loss associated with administration of triamcinolone methylprednisolone and dexamethasone These three steroids sometimes produce weight loss Sodium retention and potassium depletion occur with administration of cortisone hydrocortisone prednisone and prednisolone To prevent edema sodium should be restricted in patients receiving high doses and/or prolonged therapy with these steroids Supplemental potassium may be given in a dose of 2 Gm twice daily for adults or 0 5 Gm 3 times daily for children Excretion of both sodium and potassium occurs with triamcinolone and dexamethasone

To aid in the prevention of osteoporosis the patient on steroids should be active physically and not confined to bed for long Androgens are of questionable value

Withdrawal reactions While the steroid dose is being reduced, withdrawal reactions are apt to occur These are of 2 types

heretofore was controlled by diet, it is possible that administration of Orinase or a small amount of insulin will permit treatment with steroids

For an acute, self limited process such as contact dermatitis or drug reaction, the average adult dose, using prednisolone as a reference, is 60 mg in divided doses daily for 2 or 3 days Then the dose should be decreased by 5 mg a day until zero

For an acute exacerbation of a chronic disorder, such as atopic dermatitis, severe nummular eczema, etc, the average adult dose, using prednisolone as a reference is 40 mg in divided doses daily for 2 or 3 days After that point the dose is reduced slowly by 5 mg a day If a flare up occurs while the dose is being decreased, the patient should be maintained on the minimum effective dose Many of these patients have to be kept on 5–15 mg daily for several weeks

For severe diseases of acute onset such as lupus erythematosus and pemphigus, the adult dose, using prednisolone as a reference, varies from 60 to 120 mg in divided doses daily until a satisfactory therapeutic response is obtained The dose then should be decreased gradually by 5–10 mg daily until the minimum effective dose is reached This level should be the maintenance dose for several days or weeks If the patient is asymptomatic the dose may be lowered again

TOTAL DAILY DOSE (IN MG)
TO BE GIVEN ORALLY IN DIVIDED PORTIONS 2 TO 4 TIMES DAILY

	ADULTS	CHILDREN
Cortisone	25–300	10–100
Hydrocortisone	20–240	10–80
Prednisone	10–120	5–50
Prednisolone	10–120	5–50
Methylprednisolone	8–60	4–32
Triamcinolone	8–60	4–32
6 Fluoroprednisolone	4–30	2–16
Dexamethasone	1 5–15	0 75–7 5

Some patients will be maintained on very small amounts of these drugs e g, 5–15 mg prednisone or prednisolone, 4–8 mg methylprednisolone or triamcinolone or 1 5–3 mg dexamethasone

When patients with an acute, severe illness such as pemphigus or lupus erythematosus are receiving 60–120 mg of prednisolone daily without showing an adequate response it is often worth

while to give 100 units ACTH gel daily in addition to maintaining the oral steroid dose The clinical impression exists that ACTH preparations have a direct tropic action on the skin in addition to stimulating the production of hydrocortisone by the adrenal gland In patients on high doses of steroids by mouth the hydrocortisone output by the adrenal gland probably is nil and this situation is not changed by the administration of ACTH However the direct action of ACTH on the skin may be responsible for the beneficial effect The purified ACTH available commercially contains about 10% ACTH and 90% other materials from the pituitary gland It is not known whether the good effects stem from the ACTH or from one of the other agents present

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Withdrawal reactions While the steroid dose is being reduced withdrawal reactions are apt to occur These are of 2 types

cutaneous and systemic The former usually represent a flare up of the original dermatitis and are common when steroids are used to treat patients with chronic skin disease For these patients the steroid dose should be increased a little above that being used at the time the dermatitis began to recur After 3 to 10 days the steroid dose may be lowered gradually again with the aim of decreasing it to zero

Systemic withdrawal reactions usually are not associated with any exacerbation of cutaneous lesions These reactions include feelings of anxiety increased nervous tension, poly arthritis, vague aches and pains For these reactions the steroid dose must be increased as is done in the case of cutaneous withdrawal reactions, or the patient may be given ACTH Usually the following regimen will suffice 20–40 units of ACTH gel intramuscularly twice a week for one week then 10–20 units twice a week the second week and finally 5–10 units twice weekly the last week

Available The following chart summarizes the steroids for systemic use and their tablet sizes for oral administration Cortisone, hydrocortisone and prednisolone also are prepared for intramuscular injection Water soluble derivatives of hydrocortisone and prednisolone can be given intravenously for emergency situations

Cortisone (11 dehydro 17 hydroxycorticosterone, compound E)
5, 10, 25 mg tablets

Hydrocortisone (17 hydroxycorticosterone, compound F, cortisol)
Cortef (Upjohn), Hydrocortone (Merck)
5, 10, 20 mg tablets

Prednisone (delta 1 dehydrocortisone)
Deltasone (Upjohn) Deltra (Merck), Meticorten (Schering)
1, 2 5, 5 mg tablets

Prednisolone (delta 1 dehydrohydrocortisone)
Delta Cortef (Upjohn), Hydeltra (Merck) Meticortelone (Schering), Sterane (Pfizer)
1, 2 5, 5 mg tablets

Methylprednisolone (6α methylprednisolone)
Medrol (Upjohn)
2, 4 mg tablets

Triamcinolone (9α fluoro-16α hydroxyprednisolone)
Aristocort (Lederle) Kenacort (Squibb)
1 2 4 mg tablets
Dexamethasone (9α fluoro-16α methylprednisolone)
Decadron (Merck) Deronil (Schering), Gammacorten (Ciba)
0 5 0 75 mg tablets
Alphadrol (6α fluoroprednisolone)
Not yet commercially available

TOPICAL STEROIDS

Hydrocortisone and its derivatives in lotions creams and ointments are important in the treatment of eczematous eruptions (atopic dermatitis contact dermatitis lichen simplex nummular eczema pruritus ani etc) seborrheic dermatitis insect bites and aphthous stomatitis Cortisone and its analogues are without effect topically These agents have all but replaced the old standbys such as calamine and other shake lotions

The steroids have almost a specific effect in controlling and alleviating pruritus and in correcting the abnormal keratinizing reactions that occur with pruritus Topical steroids have no effect on the abnormal keratinization of psoriasis but they often relieve the pruritus that sometimes accompanies this disease

Steroids for topical use are available in many forms and concentrations When secondary bacterial infection is a problem it is advisable to use the preparations containing antibiotics However for general use as an antipruritic it is best not to use such preparations The application of lotions and ointments with antibiotics but without antifungal agents to body folds and creases such as the axillary inguinal and anal areas encourages the development of candidiasis

Many physicians are concerned about the possibility of absorbing topically applied steroids in sufficient quantities to produce systemic changes From a practical standpoint this is of significance only in the case of fluorohydrocortisone the salt retaining properties of which are approximately 50 times those of hydrocortisone while the anti inflammatory effect is only 10 times Absorption of topically applied fluorohydrocortisone can lead to

salt retention However, with the other steroids there is no problem On normal, intact skin a maximum of 3% of applied hydrocortisone is absorbed into the systemic circulation by trans follicular and transepidermal routes This means that 700 mg of hydrocortisone or 70 ml of 1% hydrocortisone lotion would have to be applied for 20 mg of the compound to be absorbed Because of cost, and because small quantities usually are effective, one does not apply 70 ml of hydrocortisone daily If one did absorption of 20 mg of hydrocortisone for short periods would not be particularly harmful Through damaged skin, absorption would be much greater than 3% However, the application of steroids usually brings about rapid healing of denuded surfaces resulting from eczematous eruptions so that systemic absorption decreases rapidly Through mucous membranes, which normally lack the superficial barrier of skin, absorption is about 27% In skin stripped of its outer layers following repeated application of scotch tape, approximately 85% of hydrocortisone is absorbed

Triamcinolone acetonide and fluorometholone are ideally suited for topical application because they are potent local anti inflammatory agents and yet have little effect when administered systemically Therefore, it makes no difference whether or not their topical application results in systemic absorption

There are surprisingly few complications and contraindications to the use of steroids They are not used in the presence of active cutaneous infection unless combined with antibiotics They are contraindicated in recurrent herpes simplex involving the eye On rare occasions a bacterial cellulitis or pustular eruption may follow application of topical steroids It has been our impression that topical and oral steroids given to patients with atopic derma titis predisposed them to the development of a generalized herpes simplex infection This observation has not led us to restrict the use of topical steroids in atopic dermatitis but it is a point to keep in mind when an acute eruption develops in a patient with atopic dermatitis

Application Steroids usually are available in at least 2 strengths in lotions, creams and ointments with or without antibacterial and antifungal agents Hydrocortisone free alcohol and hydrocortisone acetate are of equal effectiveness In general we

have preferred the use of lotions to creams and ointments although there are many patients who prefer the latter Although each steroid has been made available in different concentrations our choice has been 1% hydrocortisone 0 5% prednisolone 0 1% triamcinolone acetonide 0 025% fluorometholone and 0 1% fluorohydrocortisone For aphthous stomatitis the patient should keep one 20 mg tablet of hydro cortisone or one 5 mg tablet of prednisolone in the region of the ulcer once daily

Available as the following preparations

- 1% and 2 5% hydrocortisone cream and ointment in 5 10 15 20 and 30 Gm tubes with and without antibacterial and antifungal substances
- 1% and 2 5% hydrocortisone lotion in 15 and 30 ml plastic vials with and without antibiotics
- 0.5% prednisolone cream and ointment in 5, 10 and 20 Gm tubes with and without neomycin
- 0 5% prednisolone lotion in 15 and 30 ml plastic vials with and without neomycin
- 0 1% triamcinolone acetonide ointment in 5 and 15 Gm tubes with and without antibacterial and antifungal agents
- 0 1% triamcinolone acetonide cream in 5 and 15 Gm. tubes with and without antibiotics
- 0 1% triamcinolone lotion in 15 ml plastic vials with and without antibiotics
- 0 025% fluorometholone ointment in 7.5 Gm tubes with neomycin
- 0 025% fluorometholone cream in 7 5 Gm tubes

Hydrocortisone and prednisolone also are available in aerosol form

Two companies prepare water soluble derivatives of hydrocortisone and prednisolone for topical use The hydrocortisone compound is available as the diethylaminoacetate ester and is used in 0.5% concentration The prednisolone preparation is made as the phosphate and is used in 0 5% concentration Suggestions have been made that the water soluble forms of the steroids are more effective topically than the alcohol soluble derivatives

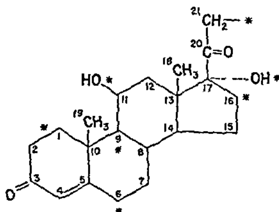
RELATIVE BIOLOGIC POTENCIES PER WEIGHT OF STEROID
(Hydrocortisone is given a reference value of 1)

	Dermatologic Effectiveness		Salt Retention and Edema	Moon Facies and Acne	Weight Gain	Osteo-porosis
	Systemic	Topical				
Cortisone	0.8	0	0.8	0.8	0.8	0.8
Hydrocortisone	1	1	1	1	1	1
Prednisone	2	0	1	2	2	2
Prednisolone	2	2	1	2	2	2
Methylprednisolone	3	4	0	3	0	3
Triamcinolone	3	4	Na excretion	4	wt loss	3
6 Fluoroprednisolone	6	7	0	*	*	*
Dexamethasone	10	10	Na excretion	*	0	*
Fluorohydrocortisone	*	10	50	*	marked	*
Triamcinolone acetonide	3	100	Na excretion	*	*	*
Fluorometholone	2	40	0	*	*	*

* Not known

However, for practical purposes there seems to be no difference in effectiveness between the water and the alcohol soluble hydrocortisone and prednisolone The hydrocortisone products are best used in 1% strength and the prednisolone products in 0 5% strength.

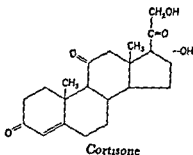
The steroids also are available in combination with tar for the treatment of eczematous eruptions with antihistamines for the treatment of pruritus and with sulfur resorcin compounds for treatment of the inflammatory aspects of acne Unfortunately none of these products has been evaluated critically Topical antihistamines usually are not recommended because of sensitizing properties



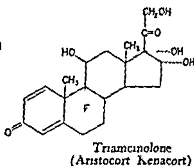
Nucleus and Numbering System Common to the Corticosteroids

The steroids available at this time are modifications of the above nucleus at one or more of the seven places indicated by asterisks.

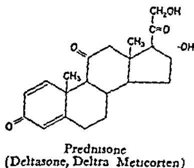
ORAL USE ONLY



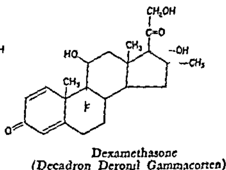
Cortisone



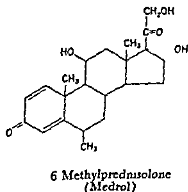
Triamcinolone
(Aristocort Kenacort)



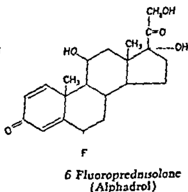
Prednisone
(Deltasone, Deltra Meticorten)



Dexamethasone
(Decadron Deronil Gammacorten)

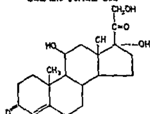


6 Methylprednisolone
(Medrol)



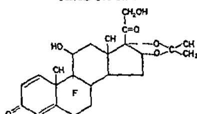
6 Fluoroprednisolone
(Alphadrol)

ORAL AND TOPICAL USE

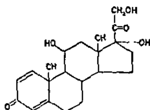


Hydrocortisone
(Cortef Hydrocortone)

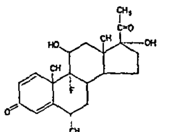
TOPICAL USE ONLY



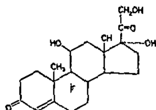
Triamcinolone acetonide
(Kenalog Aristocort acetonide)



Prednisolone
(Delta Cortef Hydeltra,
Meticortelone Sterane)

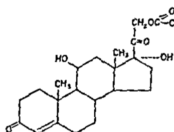


Fluorometholone
(9α Fluoro-21 desoxy Medrol,
Oxylone)

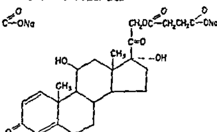


Fluorohydrocortisone
(Florinef)

WATER SOLUBLE STEROIDS
FOR INTRAVENOUS OR INTRAMUSCULAR USE

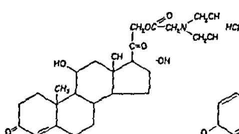


Sodium succinate ester of hydrocortisone (Solu Cortef)
For IV or IM use

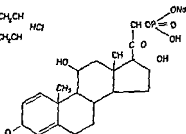


Sodium succinate ester of prednisolone (Meticortelone soluble)
For IV or IM use

WATER SOLUBLE STEROIDS
FOR TOPICAL USE IN 0 5% CONCENTRATION



Hydrocortisone diethylamino-acetate hydrochloride (Magnacort)
For topical use in 0 5% concentration

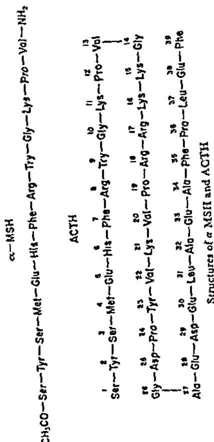


Prednisolone 21 phosphate monosodium salt (Hydeltrasol)
For topical use in 0 5% concentration

ACTH

ACTH or adrenocorticotropic hormone usually is prepared from porcine pituitary glands for parenteral administration In Europe at least one company uses ACTH obtained from whale *pituitary glands*

Structure ACTH (corticotropin, β corticotropin or corticotropin A) from the pituitary glands of hogs sheep cows and human beings is a linear polypeptide consisting of 39 amino acids The amino acid sequences in several places of the pep



Structures of α MSH and ACTH

tide chain of ACTH obtained from these four different species are identical The first 24 amino acids are required for ascorbic acid depletion activity It is not known how many of the amino acids are required for the other activities of ACTH Melano cyte stimulating hormone (α MSH) from porcine and bovine pituitary glands consists of the first 13 amino acids of ACTH, but the N terminal amino acid has an acetyl group and the

C terminal amino acid has an amide group Two porcine β MSH's consist of 18 amino acids, 7 of which have a sequence common to α MSH and ACTH The structures of porcine ACTH and α MSH are given here for comparison

Indication See the discussion under Systemic Administration of Steroids

Mechanism of Action High potency, commercially available ACTH contains approximately *10% ACTH and 90% other* polypeptides It is possible that some of the effects obtained clinically result from the non ACTH polypeptides present It is generally assumed that most of the beneficial effects obtained by giving ACTH are due to increased release of hydrocortisone from the adrenal glands However, it is likely that ACTH and/or other peptides present have a direct tropic action on the skin

On a cellular level, only 2 functions of porcine ACTH are known (1) ACTH stimulates the accumulation of cyclic adenine nucleotide which in turn activates the enzyme phosphorylase The phosphorylase enzymes which are widely distributed in tissues, catalyze reversibly the phosphorolytic splitting of α glucoside linkages of the polysaccharides, glycogen and starch to α glucose 1 phosphate, which can be metabolized further This action of ACTH on adrenal phosphorylase appears to be similar to the mechanism by which glucagon and epinephrine activate phosphorylase in the liver (2) ACTH causes darkening of melanocytes in frog skin by bringing about a reversible dispersion of pigment granules in the cytoplasm of the cells

Dose The usual dose ranges from 20 to 100 units daily For prolonged action of 12–24 hours, ACTH is given intramuscularly in a gelatin vehicle or as a zinc complex ACTH in solution is given intravenously 1 unit of ACTH gel intramuscularly is approximately equivalent in anti inflammatory effect to 1 mg of prednisolone ACTH also may be used when patients receiving high doses of steroids do not achieve the expected therapeutic effect

Available as ACTH or corticotropin in vials

Gel (Armour, National Organon Upjohn, Wilson) for intramuscular use 20 40 80 μ/ml

Zinc corticotropin (Organon) for intramuscular use 40 μ/ml

Solution (Armour National Wilson) for intravenous use 10 20 40 μ/ml

Lyophilized powder (Armour Upjohn) to be made up for intravenous use 10 25 40 μ/vial

Side effects See the discussion on steroid therapy Available ACTH preparations contain a significant quantity of melan ocyte stimulating hormones α and β MSH On prolonged administration hyperpigmentation may occur

Sweating Disorders

THE CHIEF DISORDERS OF SWEATING can be divided into 2 types (1) hyperhidrosis an abnormal increase in sweat production (2) anhidrosis, an abnormal decrease in production and/or delivery of sweat. The commonest dermatologic manifestation of anhidrosis is the sweat retention syndrome (miliaria heat rash) a result of poral obstruction which prevents sweat from reaching the skin surface

HYPERHIDROSIS

Systemic and topical agents can be used for treatment of localized hyperhidrosis Systemic medication includes anticholin ergic drugs sedatives and tranquilizers The side effects of these compounds detract from their usefulness

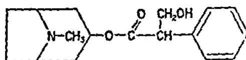
SYSTEMIC AGENTS

The anticholinergic drugs e g atropine Banthine Pro-Banthine and Pamine prevent the action of acetylcholine on the effector organs of postganglionic cholinergic nerves Hence the nerves to the sweat glands which are anatomically sympathetic but functionally cholinergic are blocked. Banthine unlike atropine also blocks the autonomic ganglia of the sympathetic and parasympathetic nervous system The action of Pro-Banthine is similar to that of Banthine but it is 2 to 5 times more potent in

its atropine like effects and about 1½ times as potent as a gang liolytic agent Also, clinically effective doses cause fewer side reactions All these anticholinergic drugs produce side effects, such as dryness of mucous membranes mydriasis blurred vision, abdominal distress, urinary retention and decreased libido

These drugs are contraindicated in the presence of glaucoma prostatic hypertrophy or cardiac failure

Belladonna Tincture, U S P

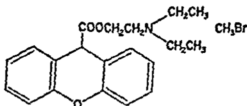


Atropine
(DL hyoscyamine)

Belladonna tincture is prepared from belladonna leaf or herb Atropa belladonna L The chief alkaloid in belladonna is L hyoscyamine, with lesser amounts of L-scopolamine (hyoscine) and possibly some atropine, which is DL-hyoscyamine, also present Atropine may be prepared from L-hyoscyamine or synthesized

Dose 6–10 drops orally 3 times daily

Banthine Bromide (Searle)



Banthine bromide
(β Diethylaminoethyl xanthene 9 carboxylate methylbromide methantheline)

Dose 50–100 mg orally 3 to 4 times daily
Available in 50 mg tablets

Pro-Banthine Bromide (Searle)

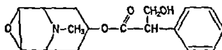
Pro-Banthine (propantheline) is similar to Banthine but has 2 isopropyl groups instead of 2 ethyl groups on the nitrogen atom.

Dose 15 mg orally 3 times daily

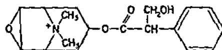
Available in 15 mg tablets which are comparable to 50 mg of Banthine

Pamine Bromide (Upjohn)

Pamine bromide is the N methylbromide (quaternary ammonium derivative) of scopolamine



Scopolamine



Pamine bromide
(Epoxytropine tropate methylbromide scopolamine methylbromide)

Dose 2 5 mg orally 4 times daily

Available in 2 5 mg tablets with or without 15 mg phenobarbital

Sedatives and Tranquilizers

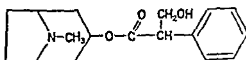
Hyperhidrosis of emotional origin is sometimes reduced through the use of sedatives or tranquilizers. The following are some examples of drugs which can be taken orally 3 to 4 times daily

Phenobarbital	15 mg
Benadryl	50–100 mg
Chlorpromazine	25–50 mg
Reserpine	0 25 mg

its atropine like effects and about 1½ times as potent as a ganglioltic agent Also, clinically effective doses cause fewer side reactions All these anticholinergic drugs produce side effects, such as dryness of mucous membranes, mydriasis, blurred vision, abdominal distress, urinary retention and decreased libido

These drugs are contraindicated in the presence of glaucoma prostatic hypertrophy or cardiac failure

Belladonna Tincture, U S P

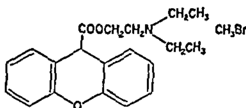


Atropine
(DL-hyoscyamine)

Belladonna tincture is prepared from belladonna leaf or herb, Atropa belladonna L The chief alkaloid in belladonna is L-hyoscyamine, with lesser amounts of L scopolamine (hyoscine) and possibly some atropine, which is DL hyoscyamine, also present Atropine may be prepared from L-hyoscyamine or synthesized

Dose 6–10 drops orally 3 times daily

Banthine Bromide (Searle)



Banthine bromide
(β Diethylaminoethyl xanthene 9 carboxylate methylbromide methantheline)

Dose 50–100 mg orally 3 to 4 times daily

Available in 50 mg tablets

Tannic Acid Lotion

Tannic acid 5%
In 70% ethyl alcohol

A variety of tannic acids is found in nature Chemically these acids are polymers of various hydroxybenzoic acids The acid commonly referred to as tannic acid is gallotannic acid the internal ester of gallic acid It is usually obtained from nutgall an excrescence on the young twigs of various species of oak trees

Indication Hyperhidrosis of feet

Mode of action Unknown

Application Apply to feet morning and night as required

Available on prescription.

Formalin, 0 25–0 5 strength

Formaldehyde (HCHO) which is a gas at room temperature, is used in the form of aqueous solutions Formalin is formaldehyde solution U S P which contains 37% formaldehyde by weight with methyl alcohol added to prevent polymerization and inactivation

Indication Hyperhidrosis of hands and feet

Mode of action Formaldehyde reacts with protein to denature it The exact relationship between this reaction and its capacity to produce anhidrosis is not known

Application Apply to palms and soles Sweating may be reduced for a period of 1 to 20 days

Caution Formaldehyde may act as a primary irritant or as a sensitizing agent.

Available on prescription

Foot Soaks

AQUEOUS

Soaking the feet in plain water for an hour or more may inhibit sweating for 8 hours probably because the terminal sweat ducts become occluded by the swollen cells of the stratum corneum.

ASTRINGENT

Astringents are drugs used locally which precipitate proteins

TOPICAL AGENTS

Aluminum Lotion

Aluminum chloride ($AlCl_3$) 10–25%
In distilled water

Indication Axillary hyperhidrosis and for prevention of odor Aluminum salts are more effective as deodorants than as antiperspirants

Mode of action Aluminum chloride, which acts as a mild epidermal irritant, produces anhidrosis by plugging the orifices of the sweat ducts so that sweat cannot escape onto the skin surface This effect does not occur in the majority of patients Aluminum compounds also decrease axillary odor associated with sweating Sterile sweat from apocrine and eccrine glands has no odor, but reaction with bacteria on the skin results in an unpleasant odor Aluminum salts have an antibacterial effect which prevents development of odor In addition they produce a chemical change which makes the usual products of bacterial decomposition in offensive

Axillary odor also can be abolished by shaving and daily washing with ordinary or antibacterial soap

Application In severe hyperhidrosis the sweat washes away the astringent so it is helpful to apply this preparation at night because emotional sweating is reduced during sleep Apply with cotton to involved areas before bedtime, allowing solution to dry for one minute Immediately thereafter, dust area with talcum powder It is advisable to begin with a 10% solution, gradually increasing it to 25% if tolerated

Caution Axillary miliaria or the sweat retention syndrome, may develop in susceptible persons In high concentration, aluminum chloride may stain clothing which comes in contact with it

Available on prescription

Indication Hyperhidrosis of nonirritated feet. This powder is stronger than the preceding one
Application Dust onto feet each morning
Available on prescription

SWEAT RETENTION SYNDROME

The sweat retention syndrome known as miliaria results from mechanical obstruction of the sweat ducts or pores within the skin so that the free outflow of sweat is prevented Heat rash (miliaria rubra) is the commonest form The most significant factor in its treatment is reduction of the need for sweating This can be brought about through proper ventilation and avoidance of exposure to heat The following medications have been used as adjuncts to this therapy

Ointments and Lotions

Ointment bases e g Eucerine and water in-oil emulsions with or without hydrocortisone may be helpful
Mode of action In the presence of excessive sweating or following application of organic solvents the keratin rings surrounding the orifices of the sweat ducts become closed Plugging of the sweat ducts leads to the formation of erythematous papules vesicles or vesicopustules This sequence of events may be reversed by applying lipid substances to the skin for lipids are required to keep the keratin rings patent Shortly after the application of a lipid to an anhidrotic area sweat may be seen emanating from the duct opening Keratolytic agents such as salicylic acid are not as effective as lipids in maintaining patency of the keratin ring

The inflammatory reaction in miliaria frequently can be controlled by topical hydrocortisone.

Powders

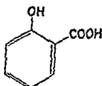
Dusting powders may offer symptomatic relief

but are so weakly penetrable that only the surface of cells is affected. Consequently, the permeability of the cell membrane is greatly reduced but the cell itself remains viable. The following astringents when used as soaks have a more prolonged effect on sweat inhibition than plain water:

1. Burow's soaks (1:40)
2. Potassium permanganate (1:2,000)
3. Tannic acid (2% in alcohol)

Powder

1. Aluminum chloride 3%
   Salicylic acid 3%
   Alum 10%
   Talcum powder 84%



Salicylic acid

$AlCl_3$
Aluminum chloride
$AlK(SO_4)_2 \cdot 12H_2O$
Alum
(Aluminum potassium sulfate)
Salicylic acid
Mg_3SiO_4
Talc
(Magnesium silicate)

Indication Hyperhidrosis and bromhidrosis of feet
Application Dust onto involved areas 1 to 3 times daily
Available on prescription

2. Tannic acid powder
   Boric acid powder
   Zinc oxide
   Equal parts of each

H_3BO
Boric acid

ZnO
Zinc Oxide

Mode of action The mechanism through which tars act on abnormal skin is unfortunately not known Clinically it can be observed that tars correct abnormalities in keratinization by decreasing epidermal proliferation and dermal infiltration It is conceivable that some of the polyphenolic substances and peroxides in tar react with and inactivate epidermal sulfhydryl groups to produce an effect on the skin similar to that resulting from exposure to radiant energy In the shale tars some of the organic sulfur compounds may be the active chemicals Tars also have vasoconstricting astringent and antipruritic properties Some but not all of the antipruritic effect is probably due to the phenols present As a rule tars exert a greater therapeutic effect if the lesions are irradiated with ultraviolet light after application of the tar Similar results are not obtained by first irradiating the tar and then applying it to the skin Apparently ultraviolet light brings about the oxidation of substances which penetrated into the skin from the tar before light exposure However when tar itself is irradiated the new compounds formed either are unstable or else cannot penetrate the skin It is possible that some of the orthoquinones and peroxides formed from the tars in irradiated skin inactivate epidermal sulfhydryl groups and thus produce a beneficial effect similar to but greater than unirradiated tar

Caution Prolonged use of some tars is associated with the production of folliculitis If folliculitis occurs topical antibiotics should be applied Because tars tend to produce photosensitization, they should not be used in such disorders as lupus erythematosus polymorphous light eruptions etc. Urinalyses should be done when tar is being applied to large areas because occasionally absorption can cause renal damage Absorption of large amounts of tar can cause gastrointestinal irritation

Coal Tar

Coal tar (pix carbonis) is obtained usually as a by product during the destructive distillation of coal Its constituents are benzene, toluene naphthalene anthracene xylene and other aromatic hydrocarbons phenol cresol and other phenolic bodies

Tar Preparations

TARS ARE DARK COLORED LIQUIDS containing mixtures of hydrocarbons and aromatic compounds obtained through destructive distillation of vegetable matter Numerous tar preparations are available, none of which can be clearly delineated because their chemical composition is not known Even tars obtained from the same source may differ from one another if prepared by different methods The term *crude coal tar* itself is not a definitive one, for although some commercial coal tars used in dermatology are prepared from anthracite coal, most of the coal tars in the eastern part of the United States are obtained from bituminous coal And on the west coast, so called crude coal tar comes from the oils derived from natural gas Add to this variability in source the fact that these tars are distilled at different temperatures and one is left with products which are highly dissimilar Tars for dermatologic use also are obtained from shales or schists, wood and petroleum

Indication Topical steroids to a great extent have replaced tar in the treatment of eczematous eruptions and pruritus However, tar is still useful for these disorders and is often the treatment of choice for psoriasis At present the coal tars are most widely used in dermatology Of the shale tars, ichthammol is very effective, being used when a tar milder than that derived from coal is indicated Wood tars, chiefly pine and juniper, are used by some Tars may be incorporated in lotions, ointments, pastes, shampoos, soaps, baths or used undiluted as varnishes The concentration of the tar prescribed must vary not only with the disorder being treated but also in accordance with the type of vehicle in which it is incorporated For example, 5% crude coal tar in petrolatum is comparable to 2% crude coal tar in a penetrating O/W or W/O base The effectiveness of tar is often increased when it is used in conjunction with ultraviolet light

Liquor Carbonis Detergens N F

Crude coal tar	200 ml
Quillaja	100 ml
95% ethyl alcohol	700 ml.

Allow to stand and filter Dilute filtrate to 1 000 ml with 95% ethyl alcohol

Quillaja is a foaming agent It is also known as soap bark Panama bark China bark or Murillo bark which is the dried inner bark of Quillaja saponaria Molina and contains quillaic acid quillajasaponin sucrose tannin and other chemicals The word quillaja is derived from the Chilean *quillean* which means to wash

For antipruritic tar baths 15–30 ml of liquor carbonis detergens may be added to the tub In shampoos 5–10% of the tar may be added It is also incorporated in lotions ointments etc

Wright's Liquor Carbonis Detergens (Fougera)

Alcoholic extract of a coal tar from England	12 8%
95% ethyl alcohol	87 2%

Available in 3 8 16 oz bottles and in 2 oz aerosol spray

BITUMINOUS SHALES OR SCHISTS

Shales are fissile rocks formed by the consolidation of clay mud or silt and have a finely stratified or laminated structure The term *schist* is applied to any metamorphic crystalline rock having a foliated structure which can be split readily into slabs

Ichthammol is a dark brown viscid liquid obtained from the destructive distillation of certain bituminous shales or schists rich in the oily residue left from fossil fish. It is sulfonated with sulfuric acid and neutralized with ammonia Ichthammol contains approximately 2 5% ammonia 8% ammonium sulfate 10% sulfur inorganic compounds as well as several hydrocarbons and aromatic substances Ichthammol is the mildest acting of the tar preparations and the only one which is water soluble It is usually too mild for use in psoriasis but is of value in inflammatory and eczematous disorders Following are some of the preparations available Ichthammol is usually best incorporated in 2–5% concentration in zinc oxide paste

ammonia, pyridine and some other organic bases Coal tar is only slightly soluble in water Approximately 3% of the coal which is heated is converted to coal tar When crude coal tar is ordered without further specification in the eastern part of the United States, the product is prepared from bituminous (soft) coal When crude coal tar is ordered on the west coast, it comes from the oils of natural gas Some commercial dermatologic tars are derived from anthracite (hard) coal

Zetar (Dermik)

Zetar is a standardized commercial product obtained from a particular type of anthracite coal which has undergone destructive distillation at 700–800° C and which is irradiated with ultraviolet light The product is specially processed with a small quantity of a surface active agent to make it easily washable with water

Zetar is available full strength for incorporation in a vehicle of one s choice It is also prepared as a 2% ointment or lotion as a 50% emulsion for tar baths and as a 1% superfatted shampoo

Kolpix A and Kolpix D (Dome)

These preparations contain the following ingredients

Coal tar A or D	2%
Zinc oxide	5%
Starch	25%
Washable base	68%

The tars A and D are obtained from bituminous coal destructively distilled at high temperatures (1,000–1,300° C) Tar A is a crude coke oven fraction and tar D a crude vertical retort fraction Each tar is derived from a different source The manufacturers claim that Kolpix A is of value in wet eczemas and Kolpix D in dry squamous eczemas

Crude Coal Tar, N F

A variety of tars is commercially available They are obtained from different sources and prepared by different methods but conform to requirements set forth in the National Formulary

of Pinus palustris Miller or of other species of Pinus It contains turpentine resin guaiacol creosol methylcreosol phenol phlorol toluene xylene and other hydrocarbons Pine tars are used in ointments in a strength of 1–5%
Pine Tar N F

Petroleum or Coal Oil

Although petroleum tars are not in common use today the derivative most widely used in the past was naphthalan obtained from Caucasian crude petroleum benzin.

Ultraviolet Light

Ultraviolet light irradiation is often used in treatment of acne vulgaris psoriasis chronic eczematous eruptions vitiligo and other skin disorders A sun bulb lamp for example RS-Westinghouse or General Electric RS costs about $10 and can be screwed into an ordinary light socket such as that of a goose neck lamp Lamps with quartz tubes can be purchased for from $50 to $150 for home use Either type of radiation source when properly used produces beneficial results Different procedures are suggested in using the 2 types because the sun lamp is much weaker than the quartz tube and longer exposure times are required

Whenever exposed to ultraviolet light the patient must protect his eyes with special sun goggles not ordinary sun glasses or with moist cotton placed over the eyes Ultraviolet light may be given every day or every other day If a sunburn develops discontinue treatment until the reaction has subsided Resume treatment at half the previous exposure time

Irradiation of the entire body surface Undress completely and lie down Place lamp so that lower edge of light source is exactly 30 in from the navel or the middle of the back.

Ichthyol (Schering)

This product, obtained from shale deposits in the Seefeld section of the Austrian Tyrol, is the material introduced by Unna in 1882

Available as Ichthyol concentrate, full strength, in 4 oz. jars, and Ichthyol ointment, 10 and 20% strengths, in 1 oz tubes.

Ichthammol, N F (Lilly, Mallinckrodt, Penick)

This includes ichthammol made from any bituminous shales or schists

Available in 10 and 20% concentrations in 1 oz tubes

Wood Tars

Wood tars are obtained from the destructive distillation of wood The source is usually juniper or pine trees and less commonly birch or beech These tars contain acetic acid but not anthracene or sulfur and are not soluble in water They are used for antipruritic baths and liniments and ointments, although very effective they are more irritating than coal tars

Juniper Tar

Juniper tar or oil of cade represents the volatile oil from the wood of Juniperus oxycedrus L Pinaceae It contains cadinene as well as other hydrocarbons and aromatic compounds

1 *Juniper Tar* N F
2 *Juniper Tar* (Almay)

This is available in the following forms an aqueous solution for antipruritic baths containing 35% juniper tar plus sulfonated oil and fatty acid esters a water washable ointment with 4% tar for topical use, a shampoo with 4% tar and a cake soap with 10% tar

Available as bath solution in 8 oz bottles, ointment in 4 oz jars, shampoo in 8 oz bottles and soap in 4 oz cakes

Pine Tar

Pine tar is obtained by destructive distillation of the wood

Irradiation of the scalp Place sheet or towel over face and put on sun goggles Cover the ears neck and other nonhairy regions. Sitting position is advisable

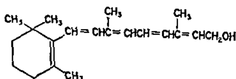
Sun lamp Place lamp 10 in above the scalp After turning on the lamp, an assistant should make multiple parts in the hair at ½ in intervals in the front and back of the scalp First exposure time is 15 seconds to each part Treat scalp twice weekly increasing exposure each time by 15 seconds up to 1 minute to each part Do not exceed 1 minute

Quartz tube Follow the directions given for the sun lamp but keep distance at 20 in rather than 10

VITAMINS AMINO ACIDS AND PROTEINS

For illnesses due to mixed or single vitamin deficiencies gratifying results are obtained by supplying the patient with the missing vitamins The situation is not clearcut when it comes to the use of vitamins for diseases that are not directly related to vitamin deficiencies For example vitamins A and C have been given for acne riboflavin and vitamin B_{12} for psoriasis PABA for scleroderma vitamin D for sarcoidosis etc In all of these cases there is no conclusive evidence that the vitamin therapy is of actual benefit In this section we will list only a few of the common vitamins reputed to be of value in some dermatoses

Vitamin A



Vitamin A

Indication Vitamin A may be of benefit in treatment of Darier s disease and ichthyosis in which conditions it is

Sun lamp Begin with exposure of 1 minute to the front and 1 minute to the back Increase exposure time ½ minute daily up to 6 minutes, front and back Then increase 1 minute daily up to 15 minutes front and back. Subsequent treatments may be continued daily without further increase in exposure time.
Quartz tube The following schedule is used

Treatment Day	Exposure Time Min	Distance of Skin from Burner In
1	¼	30
2	½	30
3	1	30
4	1½	30
5	2	30
6	2½	30
7	3	30
8	3½	30
9	4	30
10	4½	30
11	5	30
12	5	28
13	5	26
14	5	24
15	5	22
16	5	20
17	5	18

The minimum distance between the skin and the light source is 18 in After the 17th treatment day, the time factor is increased 30 seconds daily until 15 minutes is reached At this point the exposure time and distance should be kept constant

Irradiation of isolated areas Cover with cotton or linen sheets all regions outside the area to be irradiated
Sun lamp Proceed as mentioned above but keep distance at *10 15 or 20 in instead of 30*
Quartz tube Proceed as outlined in the table

Irradiation of the face Expose left side right side and front of face successively Cover eyes with special goggles or moist cotton
Sun lamp Place lamp 15 in from the tip of the nose Begin with exposure of 1 minute to each of the 3 fields Increase exposure time 30 seconds daily up to 10 minutes Then continue daily without further increase in exposure time
Quartz tube Proceed as outlined in the table



Para-aminobenzoic acid

...ra-aminobenzoic acid has been claimed to be ...se in treatment of scleroderma and dermat...s.

...t known.

...m of the potassium salt of PABA by mouth, ...ith 1 Gm. daily and increasing gradually until ...um dose is reached and then maintained. For ...se, the sodium salt of PABA is not recommended ...retention of fluid.

...Potaba (Glenwood Lab.) in 0.5 Gm. tablets or ... Gm. ampules and 100 Gm. or 1 lb. powder

...itamin D known as vitamin D_3 results from the ...raviolet light on 7-dehydrocholesterol present in ...malpighian layer of the epidermis. Vitamin D_3 ...rally in fish oils. There is no vitamin ... as calciferol is produced from ... of ergosterol, a steroid present in ... the same antirachitic activity ... chicks. Irradiation of ergosterol ... of lumisterol and tachysterol ... to dihydrotachysterol (A.T. ... y activity but little antirach... is applied to all the products ... sterol. Plants differ from ... vitamin phytosterol rather than ...

...involved in keratin formation ...n pityriasis rubra pilaris

...d tablets (Walker U S Vita...

...bullosa seem to have slowly ... DL-valine for long periods ...ino acids is the following ... from a metabolic defect ...rs and collagen have in ...up of only a few different ...table Unlike collagen ...cine and valine Since ...e no apparent collagen ... to both collagen and ...lly However the util... ...e abnormal and the ...ments of these two

H_3

CHCOOH

H_2

...aline

...uly The amino ...hemical supply ...ornia Corpora... ...l with milk or ...e costly than ...mer is used ...nsive than

applied topically For treatment of phrynoderma, pityriasis rubra pilaris and seborrheic keratoses, vitamin A has been used both orally and topically

Mode of action In phrynoderma, vitamin A is given orally to compensate for a vitamin deficiency In this case it acts as a replacement for a substance lacking in the diet. In Darier's disease, ichthyosis and phrynoderma, topically applied vitamin A may cause inhibition of epidermal sulfhydryl groups, which are required for keratin formation, and not be a vitamin supplement for a specific metabolic process.

Caution Toxic effects from overdosage or prolonged systemic administration of vitamin A include anorexia, weakness headache exophthalmos, hepatomegaly, splenomegaly, bone and joint tenderness, alopecia and ecchymoses

Dose *Topical—50,000–100 000 units (1 5–3%)* vitamin A per gram of Neobase or Lubriderm applied once or twice daily

Oral—50,000–150 000 units daily

Available as synthetic vitamin A, 50,000 units per capsule or tablet, from several pharmaceutical companies

Vitamin B

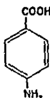
Vitamin B Complex

Indication Vitamin B complex is used in the treatment of pellagra, cheilitis and chronic debilitating dermatoses such as pemphigus and exfoliative erythroderma

Mode of action The vitamins of the B complex act as coenzymes for energy yielding metabolic reactions These vitamins must be added to the diet of patients suffering from vitamin B deficiency or whose nutritional requirements are in excess of normal

Dose 1–2 capsules daily by mouth depending upon concentration per capsule Numerous commercial preparations are available

PABA



Para aminobenzoic acid

Indication Para aminobenzoic acid has been claimed to be of possible use in treatment of scleroderma and dermatitis herpetiformis

Mode of action Not known

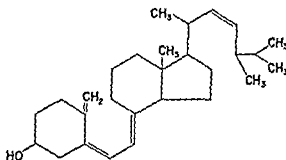
Dose 8–15 Gm. of the potassium salt of PABA by mouth beginning with 1 Gm daily and increasing gradually until the maximum dose is reached and then maintained For prolonged use the sodium salt of PABA is not recommended because of retention of fluid

Available as Potaba (Glenwood Lab) in 0 5 Gm tablets or capsules 2 Gm ampules and 100 Gm or 1 lb powder

Vitamin D

Natural vitamin D known as vitamin D_3 results from the action of ultraviolet light on 7 dehydrocholesterol present in milk or the malpighian layer of the epidermis Vitamin D_3 also occurs naturally in fish oils There is no vitamin D_1 Vitamin D_2 known as calciferol is produced from ultraviolet light ir radiation of ergosterol a steroid present in yeast Vitamin D_2 has almost the same antirachitic activity as vitamin D_3 in rats but less in chicks Irradiation of ergosterol also results in the formation of lumisterol and tachysterol The latter can be reduced to dihydrotachysterol (A T 10) which has much antitetany activity but little antirachitic effect The term *viosterol* is applied to all the products resulting from irradiation of ergosterol Plants differ from yeasts and animals in that they contain phytosterol rather than ergosterol or 7-dehydro-

cholesterol In treatment of skin diseases, calciferol is used more often than vitamin D_2 because it is readily available in pure form



Vitamin D_2
(Calciferol)

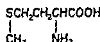
Indication Calciferol is used for treatment of lupus vulgaris and is of possible use in parapsoriasis

Mode of action Unlike bacteriostatic and bactericidal chemotherapeutic agents calciferol has no direct effect on the tubercle bacillus but stimulates the reaction of the host to the organism so that fibroblastic activity is increased

Caution Nausea, vomiting, headache and kidney damage may occur Serum calcium levels should be checked frequently

Dose 50,000–150 000 units daily by mouth Numerous commercial preparations are available

DL Methionine



Methionine

Methionine is an amino acid essential for the growth of the white rat and for the maintenance of nitrogen balance in the young adult Methionine can be converted to cysteine which subsequently can be changed to cystine Through these re

actions methionine probably is involved in keratin formation

Indication May be effective in pityriasis rubra pilaris

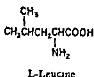
Mode of action Not known

Dose 1-2 Gm 3 times daily

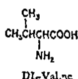
Available in 0 5 Gm capsules and tablets (Walker U S Vitamin Ives Cameron)

L Leucine and DL Valine

Some infants with epidermolysis bullosa seem to have slowly improved when fed L-leucine and DL-valine for long periods The rationale for giving these amino acids is the following Epidermolysis bullosa may result from a metabolic defect involving elastic fibers Elastic fibers and collagen have in common the property of being made up of only a few different kinds of amino acids as shown in the table Unlike collagen elastin contains large amounts of leucine and valine Since patients with epidermolysis bullosa have no apparent collagen deficiency the amino acids common to both collagen and elastin probably are metabolized normally However the utilization of leucine and valine might be abnormal and the patient may benefit from daily supplements of these two amino acids



L-Leucine



DL-Valine

Dose 1 Gm of each amino acid by mouth daily The amino acids in powder form available from biochemical supply companies (Nutritional Biochemicals or California Corporation for Biochemical Research) may be mixed with milk or some food the baby likes L-leucine is no more costly than DL-leucine and for this reason the natural isomer is used However DL-valine is considerably less expensive than L-valine so the racemic mixture is given

PER CENT COMPOSITION IN ROUND FIGURES OF AMINO ACIDS IN COLLAGEN AND ELASTIN

AMINO ACID	COLLAGEN	ELASTIN
Glycine	30	30
Proline	15	15
Hydroxyproline	15	2
Alanine	10	20
Aspartic acid	10	1
Arginine	10	1
Glutamic acid	10	2
Leucine	4	10
Valine	2	20

Plain Gelatin (Knox)

Gelatin is a protein obtained by boiling skin tendons ligaments, bones, etc, with water Eighty nine per cent of its composition is derived from 6 amino acids which are present in the following approximate percentages

Glycine	27%
Proline	17%
Hydroxyproline	15%
Alanine	11%
Aspartic acid	10%
Arginine	9%

Indication Brittle nails

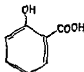
Mode of action The mechanism of action is unknown, but it is possible that gelatin provides the optimal amount of an amino acid required for normal nail formation Although glycine is the amino acid present in the greatest amount, it is not solely responsible for the efficacy of gelatin because administration of large doses of glycine alone does not cause improvement of brittle nails

Dose 7 Gm (¼ oz envelope) by mouth daily for 3 months The gelatin may be mixed with water, fruit juice or some other beverage Gelatin also is available in capsules in which form it is easier to swallow However the dose advertised for capsules is usually very small, and the capsules are considerably more expensive than plain gelatin

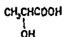
Wart Removers, Keratolytics and Caustics

Sal Lac in Flexible Collodion

Salicylic acid 10%
Lactic acid 10%
In flexible collodion



Salicylic acid



Lactic acid

Flexible collodion consists of 2% camphor and 3% castor oil in collodion Collodion contains 4% pyroxylin (chiefly dinitrocellulose) in a solution made up of 1 volume of absolute ethyl alcohol and 3 volumes of diethyl ether

Indication Common wart (verruca vulgaris) May be used for flat warts (verrucae plana) if concentrations of salicylic and lactic acids are reduced to 5% each

Mode of action Salicylic and lactic acids act corrosively on warts Collodion keeps these caustic agents in contact with the wart and also delimits their zone of *activity*

Application This preparation is applied to the *wart surface* with a toothpick and allowed to remain for 24 hours It is then peeled off and a fresh application is made This procedure is followed for 3 weeks If soreness develops 2-day intervals should be allowed between applications Children s skin may become irritated after a single application For children use 5% each of salicylic acid and lactic acid in flexible collodion instead of 10%

Available on prescription.

Formaldehyde in Aquaphor

40% formaldehyde	4 ml
Aquaphor	15 Gm

HCHO
Formaldehyde

Indication Common and plantar warts (verrucae vulgaris and plantaris)

Mode of action Formaldehyde acts corrosively on warts

Application Apply sparingly to warts, using a small applicator such as a toothpick once daily As lesions become firm, remove the hardened keratin by paring gently with a razor blade Reapply preparation This procedure should be carried out once daily for 3 to 4 weeks or until disappearance of the warts

Available on prescription

Salicylic Acid Plaster (Duke)

Salicylic acid	40%
In elastic adhesive plaster bandage	

Indication Plantar warts and calluses

Mode of action Salicylic acid in 40% concentration acts corrosively on tissue

Application The plaster should be cut to conform to the size of the lesion over which it is then placed and allowed to remain for 2 days The plaster is then removed after which the foot is soaked in water for ½ hour and the hyperkeratotic lesion scraped with a scalpel or razor blade New plaster is then applied 2 to 4 such applications should be sufficient If lesions recur, re treatment may be necessary

Carbon Dioxide (dry ice)

Indication Plantar wart

Mode of action When solid carbon dioxide which has a temperature of approximately $-78°$ C is applied to a wart for a sufficient period of time the wart as well as some adjacent normal tissue becomes devitalized

Application Solid carbon dioxide in the form of a pencil or disc is applied to the lesion with firm pressure for 3 to 5

minutes The shape and area of the carbon dioxide used should conform exactly to the contour of the wart Carbon dioxide must not be allowed to come in contact with normal skin Within 2 or 3 days a deep vesicle forms beneath the wart so that the wart may be excised easily by using a scalpel or scissors without anesthesia An antibiotic ointment or powder should be applied to the wound which should then be dressed with an elastic adhesive bandage

Solid carbon dioxide may be formed in small plastic tubes of various diameters upon the sudden release of carbon dioxide gas into the tubes A portable unit (Kidde) is available or one can direct carbon dioxide gas from a large cylinder into the small plastic tubes using an adapter designed by Stolar Solid carbon dioxide also may be obtained from local dairies

Liquid Nitrogen (N)

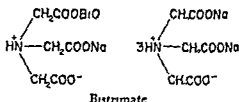
Indication Common wart

Mode of action Liquid nitrogen boils at a temperature of −196 C When applied to a wart it destroys the lesion through freezing Because it is much colder than dry ice liquid nitrogen is more effective and requires a shorter time of application

Application The wart should be pared before liquid nitrogen is used A cotton tipped applicator is dipped in the liquid nitrogen and then applied to the wart rapidly and with light pressure A temporary burning sensation may occur after contact with the liquid nitrogen and some discomfort may be present for 24 hours. A deep vesicle usually develops at the base of the wart within 1 to 3 days At this time without local anesthesia the lesion may be lifted up with forceps and excised at the base with scalpel or scissors

Bistrimate Tablets (Smith Carrol Dunham)

Bistrimate consists of sodium bismuth triglycollamate com bined with 3 equivalents of disodium triglycollamate to form a double saltlike compound



Bistrimate

Indication It has been claimed that bistrimate is of value in the treatment of flat and common warts, although one *statistical study showed no difference between treated and* control groups

Mode of action Unknown It is possible that psychotherapy associated with administration of tablets is a factor

Dose Initially, 1 tablet by mouth 3 times daily after meals for *2 to 3 days then 2 tablets 3 times daily for 3 to 4 weeks*

Available as tablets each containing 410 mg of sodium bismuth triglycollamate, which is equivalent to 75 mg of elemental bismuth

Side effects Aphthous stomatitis and renal damage Urinalyses *should be followed*

Podophyllin

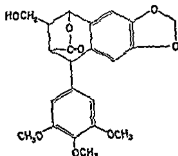
Podophyllin can be prepared in any of the following forms

1	Podophyllin powder Suspended in mineral oil	20–25%
2	Podophyllin solution In 95% ethyl alcohol	20%
3	Podophyllin In an ointment base	20%

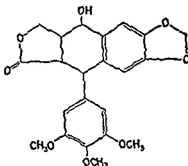
Podophyllin, the common name for podophyllum resin, is obtained from the rhizome and roots of the herb, mandrake (may apple) The active ingredients are podophyllotoxin and picropodophyllin Inactive chemicals present include picropodophyllic acid, podophyllic acid and podophylloquercetin

Indication Venereal warts (condylomata acuminata) Has also been used for seborrheic keratoses

Mode of action Unknown Podophyllin appears to be specific for treating venereal warts and is not very effective in removing other types



Podophyllotoxin



Picropodophyllin

Application The skin surrounding the lesion to be treated should be protected with zinc oxide paste The podophyllin preparation is then applied In 6–12 hours the treated lesion should be washed in order to remove the podophyllin A few hours after application to venereal warts the lesions become blanched In 24–48 hours they appear necrotic. On the 3d day they begin to slough and then disappear without scarring The recurrence rate is approximately 15% Surgical destruction of recurrent lesions has been advocated in some cases.

Available on prescription

Other Corrosive Substances

Many other corrosive substances, such as trichloroacetic acid (25% in water to full strength), euphorbia resin (milk weed), fuming nitric acid, etc, are at times effective in the treatment of warts However, care must be taken in their application because unsightly keloids sometimes develop

Salicylic Acid Ointment

Salicylic acid 5–10%
In an ointment base

Indication Localized hyperkeratosis, such as keratosis of the palms and soles This preparation also can be used to remove the surface of thin milia
Mode of action Salicylic acid is keratolytic in this concentration range
Application Apply twice daily to involved areas
Available on prescription

Silver Nitrate

10 or 25% silver nitrate in water
or
silver nitrate applicator stick
(Clay Adams Arzol Chemicals Tappan Zee)

The sticks are composed of about 75% silver nitrate and 25% potassium nitrate
Indication Silver nitrate can be used in solution or as an applicator stick to destroy excess granulation tissue and to cauterize fissures and ulcers in order to stop weeping
Mode of action Silver nitrate acts as a caustic by coagulating tissue protein, thereby stopping oozing and allowing for epithelization
Application Silver nitrate solutions should be applied to the involved areas with a cotton tipped applicator The stick should be moistened with water before use Fissures and ulcers may be touched lightly but granulation tissue requires exertion of pressure when the silver nitrate is being applied

Wet Dressings

WET DRESSINGS which consist of bandages soaked in mineral solutions are applied to involved areas and either left open or enclosed in a water tight covering such as plastic waxed paper or oiled cloth The open type of dressing is used more frequently in dermatologic therapy The systemic use of steroids concomitantly with topical wet dressings has greatly shortened the time required to achieve a beneficial effect

Indication Open wet dressings are used to soothe and cool superficial inflammation to dry weeping or oozing lesions to cleanse crusts to drain and treat infected areas and to relieve pruritus. Closed wet dressings may be used when it is desirable to retain heat rather than permit evaporation and cooling Also they promote maceration of the skin Soothing solutions for acute lesions are aluminum acetate preparations In the presence of marked weeping silver nitrate or potassium permanganate is preferred For skin infections due to bacteria, wet dressings made with silver nitrate potassium permanganate or antibiotics are indicated For mycotic infections, potassium permanganate is the agent of choice

Mode of action Wet dressings have a soothing and antipruritic effect on inflamed skin and a cleansing action as well When they are left open cooling occurs through evaporation of water When they are closed water cannot evaporate and heat is retained Through the prolonged soaking inherent in closed dressings maceration occurs The active agents in wet dressings such as silver nitrate aluminum acetate lead acetate and potassium permanganate precipitate proteins and through this mechanism lead to suppression of weeping The action of potassium permanganate is due to its oxidizing properties The antibiotic wet dressings as well as the preceding ones are germicidal

Application Soft cloths such as old handkerchiefs bed linen Kerlix or soft gauze fluffs are used for wet dressings Gauze

squares are contraindicated because of their tendency to come apart and to adhere to the skin and cause irritation Each digit should be wrapped separately Special gloves called Dermpak are useful in applying wet dressings to the hands The bandages should be removed, moistened and reapplied every 5–10 minutes for 1 to 2 hours 3 times a day so that the dressings do not dry out If it is not possible to carry out this preferred technique, wet dressings may be changed every 2 or 3 hours during the day by removing them completely, soaking and reapplying Dressings should not be re moistened while on the patient because it is difficult to wet the bandages evenly and also because complete re soaking is necessary to remove accumulated detritus During the intervals when wet dressings are not being used, a lotion, liniment or paste may be applied The solutions should be lukewarm If they are too hot, vasodilatation resulting in weeping and itching occurs If they are cold, vasoconstriction occurs, which relieves warmth and pruritus temporarily, but reactive vasodilatation develops

Wet dressings should be covered with porous cotton tubing or terry cloth towels to allow for evaporation Plastic, waxed paper, oiled silk or rubber should not be used unless the effects of a closed dressing are desired It is a good idea to use plastic or some other impermeable material to separate the mattress from the bed linen underlying the part of the body being treated A cradle to hold the bedding off the affected part is helpful A bed cradle for home use may be constructed from large boxes opened at one end These can be fastened with rope to the foot or springs of the bed The bandages should be changed daily because they become saturated with body secretions and will not hold the treatment solutions The used dressings, particularly if they are Kerlix bandages, may be laundered and used again rather than discarded

Aluminum Acetate

Many preparations containing aluminum acetate are used for wet dressings In different parts of the world the name *Burow's solution* has been applied to several mixtures of dissimilar pH which contain aluminum acetate in varying

amounts which may or may not also include lead acetate

$Al(CH_3COO)_3$ Aluminum acetate	$Al_2O(CH_3COO)_4 \cdot 4H_2O$ Aluminum subacetate
$Pb(CH_3COO)_2 \cdot 3H_2O$ Lead acetate	$Al_2(SO_4)_3 \cdot 18H_2O$ Aluminum sulfate
$Ca(CH_3COO)_2 \cdot H_2O$ Calcium acetate	$CaCO_3$ Calcium carbonate

Following are the most frequently used aluminum acetate preparations

1 Burow s Solution U S P

Burow s solution described in the United States Pharma copeia is also known as aluminum acetate solution and contains approximately 5% neutral aluminum acetate

Aluminum subacetate solution	545 ml
Glacial acetic acid	15 ml
Dilute with water to make	1 000 ml

Up to 0 6% boric acid may be added to prevent precipita tion of a basic compound which forms on standing

For use as a wet dressing the stock solution must be diluted 1 16 1 20 or 1 32

Final Strength	Burow's Stock Sol.	Water to Dilute
1/16	30 ml (1 oz)	1 pt.
1/20	30 ml (1 oz.)	1¼ pt
1/32	15 ml. (½ oz)	1 pt

2 Burow s Solution With Lead Acetate

Aluminum acetate	87 Gm
Lead acetate	150 Gm
Water to make	1 000 ml.

For use as a wet dressing the stock solution must be diluted 1 16 1 20 or 1 32, as shown above

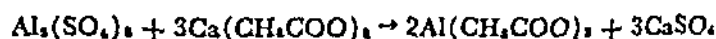
3 Aluminum Subacetate Solution U S P

Aluminum sulfate	160 Gm
Acetic acid	160 ml
Precipitated calcium carbonate	70 Gm.
Water to make	1 000 ml.

Dilute 1 16 1 20 or 1 40 as described above.

4 DOMEBORO TABS AND POWDER (Dome)

Effervescent tablets or packaged powder can be used con veniently by nonhospitalized patients to prepare aluminum acetate solution Each packet contains 2 2 Gm of powder or a 2 2 Gm tablet made up of 60% aluminum sulfate 38% calcium acetate and 2% boric acid The boric acid is used to buffer the preparation to pH 4 2–4 5 In addition, each tablet contains sodium bicarbonate for easy solubility through effervescence When the tablet or powder is dis solved in water, the following reaction occurs so that fresh aluminum acetate is available for use



$$Al_2(SO_4)_3 + 3Ca(CH_3COO)_2 \rightarrow 2Al(CH_3COO)_3 + 3CaSO_4$$

Dissolve the contents of 1 packet in 1 pt of water for a 1 20 solution of aluminum acetate

Silver Nitrate ($AgNO_3$)

Silver nitrate can usually be obtained in a 10 or 25% stock solution For wet dressings this should be diluted so that the final concentration of silver nitrate is 1 750 or 1 1,000 Ordi nary tap water can be used provided its chloride content is low In localities where such water is not readily available, distilled or demineralized water must be used

FINAL STRENGTH	$AgNO_3$ STOCK SOL 15 ML (½ OZ)	WATER TO DILUTE
1/750	10%	1 qt
	25%	2½ qt
1/1 000	10%	1½ qt
	25%	4 qt

Silver nitrate stains clothing and skin Stains may be re moved either by first moistening with iodine (2%) and then washing immediately with water or by applying a 10% solution of potassium iodide and then removing the resulting yellow color with thiosulfate solution

Potassium Permanganate ($KMnO_4$)

Potassium permanganate is usually available in 65 or 300 mg (1 or 5 gr) tablets A fresh solution must be made up

for each application by crushing the tablet to a fine powder between 2 tongue blades and then dissolving the powder in water Solutions of 1 4 000 or 1 9 000 strength are used

Final Strength	$KMnO_4$ Tablets	Water to Dilute
1/4 000	65 mg (1 gr)	½ pt
	330 mg (5 gr)	1½ qt
1/9 000	65 mg (1 gr)	1 pt
	330 mg (5 gr)	3 qt

Potassium permanganate stains skin clothing and tub Stains can be removed with dilute sulfurous or oxalic acids or *hyposulfite solutions*

Antibiotics

Wet dressings can be prepared by dissolving the indicated quantity of antibiotic in saline Neomycin has greater stability than the other antibiotic wet dressings

1 Bacitracin
   Gram positive bacteria gonococcus meningococcus
   100 units bacitracin per ml saline
   Available as dry powder in 2 000 10 000 and 50 000 unit vials
2 Neomycin Sulfate
   Gram positive and gram negative bacteria M tuberculosis
   2 mg neomycin per ml saline
   Available as powder in 500 mg vials
3 Polymyxin B Sulfate
   Gram negative bacteria including pyocyaneus but not proteus
   1 mg polymyxin per ml saline
   Available in 20 mg vials

Magnesium Sulfate (Epsom salts $MgSO_4$ $7H_2O$)

For wet dressings prepare a 1 65 solution by dissolving 1 tablespoon per qt. of water

Dalibour Solution

A 1 16 dilution can be prepared by dissolving the contents

4 Domeboro Tabs and Powder (Dome)

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of one 2 2 Gm packet in 1 qt of water The composition of undiluted Dalibour solution is

Zinc sulfate	2 25%
Copper sulfate	0 65%
Camphor	0 10%

Available as Dali Sol powder (Dome) in 2 2 Gm packets

Physiologic Saline (0 86% NaCl)

Physiologic saline is a mild but relatively inactive solution for wet dressings which can be prepared by dissolving 1 level tsp of table salt in 1 pt of water

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